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NATIONAL AMBIENT AIR QUALITY OBJECTIVES FOR GROUND-LEVEL OZONE

SCIENCE ASSESSMENT DOCUMENT

A report by the
Federal - Provincial Working Group
on Air Quality Objectives
and Guidelines

JULY 1999

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Part 1 of 7

Canada

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PREFACE

The Canadian Environmental Protection Act (*CEPA*), passed into law in 1988, replaces and builds upon the Clean Air Act and the Environmental Contaminants Act. The opening statement of the Act declares that "the protection of the environment is essential to the well-being of Canada". *CEPA* allows the Federal Government to assess substances and control their impact through national environmental quality objectives, guidelines, codes of practice, and/or regulations.

Provincial Governments have the primary responsibility in many areas of air pollution control, with federal actions integrated with those of the provinces. The *CEPA* Federal/Provincial Working Group on Air Quality Objectives and Guidelines (WGAQOG), consisting of representatives of federal, provincial and territorial departments of environment and health, reviews and recommends national ambient air quality objectives.

Canada's *National Ambient Air Quality Objectives(s) (NAAQOs)* prescribe targets for air quality, measured at the relevant receptor (persons, plants, animals, materials). *National Ambient Air Quality Objectives are national goals*[1] *for outdoor air quality that protect public health, the environment, or aesthetic properties of the environment.* The development of NAAQOs involves first, a scientific review of the physical and chemical properties of a substance, its sources, environmental, animal and human health effects, and an assessment of environmental and human exposure to the substance. Secondly, this information is integrated within a framework of risk assessment. The Science Assessment Document contains this critical scientific evaluation, and lays the scientific groundwork for establishing the air quality objectives. Reference Levels, levels above which there are demonstrated effects on human health and/or the environment, are identified. A document outlining the process followed in reviewing and interpreting the scientific information is published separately.[2] This document contains the scientific evaluation of Ground Level Ozone.

National Ambient Air Quality Objectives are targets for focussing air quality management strategies and plans. The derivation of these targets may consider some elements of benefit/risk analysis, reflecting a philosophy of environmental health protection and long term risk reduction while recognizing technological and economic limits. The broad range of potential responses by ecosystems, populations, and organisms in the environment are considered. Given the range of sensitivities within and among these environmental components, the resulting objectives may not protect all.

The process of establishing National Ambient Air Quality Objectives is a dynamic and continuous one. Air quality objectives are established to reflect the current state of knowledge about an air pollutant, to provide a national indicator for assessing the quality of air in all parts of Canada, and to provide guidance to governments for making risk management decisions such as planning control strategies and setting local standards.

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[1] The Working Group develops NAAQOs for Federal/Provincial/Territorialand Municipal Governments to use as they deem appropriate. Implementation of air quality management strategies and standards is left to those agencies or to other national processes.
The definition in the text above, along with the descriptor provided above in this footnote, together comprise the new definition for NAAQOs.

[2] A Protocol for the Development of National Ambient Air Quality Objectives Part 1: Science Assessment Document and Derivation of the Reference Levels. WGAQOG, 1996.

It is recognized that not all locations in Canada will meet these air quality objectives immediately, or at all times, and that priority given to meeting these values may be based on factors such as available control technology, costs, benefits, and the degree to which the recommended objectives are exceeded. The expectation is that strategies will be implemented to facilitate the reduction of ambient air concentrations to a level at or below the air quality objective(s) as soon as practicable. The principles of continuous improvement and nondegradation of environmental quality are advocated.

NOTE:
In January 1998, Canadian Environment Ministers (with the exception of Québec) signed the Canada-Wide Accord on Environmental Harmonization and its sub-agreement on Canada-Wide Standards (CWSs). The CWS process provides new tools for the management of environmental issues of national interest. Recognizing that both NAAQOs and CWSs have a role to play in the management of air quality, federal, provincial, and territorial health and environment departments have integrated the NAAQO and CWS processes. Air pollutants that have been identified by governments as needing to be managed will be targeted for either CWS or NAAQO development, not both.

In January 1998, Environment Ministers identified ozone as a priority for Canada-Wide Standards. As a result, federal, provincial, and territorial health and environment departments agreed that NAAQOs for ozone will no longer be developed. Rather, this Science Assessment Document will form the Risk Assessment report for the development of CWSs for ozone.

NOTE:
This Science Assessment Document is, in general, a federal-provincial consensus document. One member of the WGAQOG, Alberta, does not, however, support some of the recommendations, including the form of the LOAEL for vegetation and the recommended Reference Levels for Human Health. This position is based on issues regarding the science and its application with respect to ozone impacts on health and the environment. Alberta nevertheless supports the publication of this document and believes that this document will make a positive contribution to the efforts of reducing ambient ozone levels in Alberta. More information on Alberta's position can be obtained from Alberta Environment, Environmental Sciences Division at (780) 427-5883 or from www.gov.ab.ca/env/protenf.html .

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- Ground-level ozone and it precursors, 1980 - 1993: Report of the Ambient Data Analysis Working Group (1997)
- Ground-level ozone and precursor monitoring guidelines and implementation plan: Report of the Ambient Air Monitoring Working Group (1997)
- Report of the Health Objective Working Group (1997)
- Report of the Vegetation Objective Working Group (1997)

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1 INTRODUCTION

The material contained within this report presents the current scientific and technical information relevant to the review of the present Canadian National Ambient Air Quality Objectives (NAAQOs) for ground-level ozone in air. This document has been prepared primarily as a compilation of the 1996 NO_x/VOC Science Assessment reports prepared under the auspices of the Multistakeholder NO_x/VOC Science Program. This material was augmented by an assessment of more recent literature on the human health effects of ozone, and the addition of material on the effects of ozone on materials and on animals. Recent literature on ozone effects on vegetation was also reviewed, but in consideration of the finding that there was no cause to alter the conclusions of the NO_x/VOC report on vegetation effects, the material was not updated. The information in this Science Assessment Document is based upon peer reviewed and publicly available information. The updated effects information is current to mid 1997. The individual reports which have been drawn upon for this assignment include:

- Ground-level ozone and its precursors, 1980-1993 — Report of the Data analysis Working Group (Multistakeholder NO_x/VOC Science Program, 1997)
- Ground-level ozone and precursor monitoring guidelines and implementation report—Report of the Ambient Air Monitoring Working Group (Multistakeholder NO_x/VOC Science Program, 1997)
- Report of the Health Objective Working Group (Multistakeholder NO_x/VOC Science Program, 1997)
- Report of the Vegetation Objective Working Group (Multistakeholder NO_x/VOC Science Program, 1997)
- National Air Pollution Surveillance Network Quality Assurance and Quality Control Guidelines (Mar, 1995)
- Canadian Emissions Inventory of Criteria Air Contaminants (1990) (Environment Canada, 1996)

The current Canadian Ozone Maximum Acceptable Air Quality Objective, developed in 1976 under the old three-tiered Framework for NAAQOs, is 82 ppb (parts per billion) with a one hour averaging time. This was reviewed in 1989 under the Canadian Environmental Protection Act (CEPA) and confirmed based upon the information available at that time.

This report constitutes the Science Assessment Document for ozone, which lays the foundation for the Risk Characterization and presents the rationale for the Reference Levels. Subsequent processes will develop the NAAQO(s) by considering technical, economic and social factors along with the scientific information as appropriate and feasible. The text is organized as follows:

- An introduction (1) provides contextual background information with following chapters on atmospheric chemistry (2), sampling and monitoring methods (3), and sources of ozone and its precursors to the environment (4).
- Chapter 5 summarizes the information on ambient environmental levels of ground-level ozone for remote, urban and rural monitoring stations, and discusses the factors contributing to ozone episodes.
- Chapters 6 through 11 present the scientific and health based information on exposure (6), the effects of ozone on materials (7), vegetation (8), birds and mammals (9), and on humans (10-12).
- The derivation of Reference Levels and the Risk Characterization are provided in Chapters 13 and 14.

The development of ambient air quality objectives for ground-level ozone is a difficult task due to the existence of identifiable and quantifiable impacts to more than one receptor: human health, vegetation and materials. The management of ground-level ozone is complicated by the fact that it is the product of complex secondary atmospheric chemical reactions.

Virtually none of the ground-level ozone measured in air is directly emitted from biogenic (natural) or anthropogenic (human) sources. Ozone is the product of a complex series of chemical reactions involving nitrogen oxides (NO_x) and volatile organic compounds (VOC). These primary pollutants, also known as precursor gases, are the products of combustion processes often associated with industry and the transportation sector. Some NO_x and VOC may be produced by biogenic sources, especially in summer when emissions from natural vegetation and agricultural crops, as well as associated management practices, are highest.

Local and regional meteorology are important factors in evaluating the severity and origin of ozone episodes, which tend to be associated with inversion conditions (which limit the dispersion of pollutants) and higher air temperatures and solar radiation from May through September.

Since high population density urban environments produce high levels of NO_x and VOC from transportation, ground-level ozone episodes are often most pronounced near these urban centres. In Canada, three areas have been identified as having excessively high numbers of days per year with ozone concentrations above the current NAAQO of 82 ppb. These are the Vancouver–Lower Fraser Valley area, where local physiography traps ozone during inversions; the Windsor-Québec City corridor (along the U.S. border and St. Lawrence River); and the southern Atlantic region. The latter two areas experience significant contributions due to long range transport of ozone and its precursors from the eastern and central or mid-west United States.

Since ground-level ozone co-exists in the atmosphere with other air pollutants prevalent in the urban environment, it is important to determine whether ozone acts alone or in combination with other common pollutants in affecting receptors. As this issue is not fully resolvable given current scientific understanding, this assessment will address only direct ground-level ozone receptor responses.

The effect of ozone on plants occurs when ozone enters the plant leaves disrupting oxidative photosynthesis processes and energy budgets of the plant, affecting leaves and roots. Damage to agriculture crops from ozone has been documented in Canada and the United States since the 1950s. Damage to forests near areas of high ozone concentration has also been reported. The effects of ozone on agricultural crops has been studied extensively, with highly variable sensitivities being reported due to differences in plant species, cultivars and growing conditions.

Effects of ground-level ozone on human health include reduced lung function, increased symptoms of respiratory discomfort and disease, and increased hospitalizations and emergency department visits, and death. There is evidence that ozone and particulate matter may act together in affecting human health when levels of both are elevated. Respiratory tract inflammation caused by ozone may predispose the tissue to the effect of particles. As with plants, there is wide variation in the response of the individual to ozone, with asthmatics being particularly sensitive.

A variety of materials have been shown to be susceptible to damage from exposure to ozone, including elastomers, textiles, painted surfaces, metals and masonry. Effects on metals and masonry are thought to be primarily the result of synergistic effects with sulphur dioxide. Cracking, fading, erosion and/or corrosion of materials are the principle effects observed.

There is relatively little information available on the effects of ozone on wildlife. The only significant exposure route is inhalation and therefore, the primary effects, as with humans, are respiratory. Indirect effects are also possible; for example ozone may affect the plants upon which wildlife feed.

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2 ATMOSPHERIC CHEMISTRY

The information in this chapter is based primarily on that presented in the Report of the Data Analysis Working Group (Multistakeholder NO_x/VOC Science Program, 1997).

2.1 CHEMICAL PROPERTIES

Ozone is a colourless gas at ambient air concentrations. In its pure, undiluted form the gas has a dark bluish colour. The three oxygen molecules are linked at an angle of 116°49'±30' with a distance between the atoms of 1.278±0.003Å. The basic physical properties of ozone are listed in Table 2.1 (Lide, 1996).

Table 2. 1 Physical and Chemical Properties of Ozone

Physical State	Gas
Physical Description	Coloured gas with pungent odour
Molecular Formula	O_3
Melting Point	-192.7±2°C
Boiling Point	-111.9°C
Density gas liquid	 2.144 gm/l @ 0°C 1.614 gm/l @ -194°C
Water Solubility	$49cm^3$ @ 0°C
Vapour Pressure	1mm Hg @ -180.4°C
CAS Number	10028-15-6
Henry's Law Constant	$4.57x10^{-3}$ @ 20°C
Molecular Weight	47.9982
Common Valences	4 primary structures with strong delocalized π bonding
Rate Constants	
Photolysis Oxidation/photo-oxidation Hydrolysis	Complex, see Section 2.2

Ozone is a strong, gaseous oxidizing agent which reacts rapidly with other atmospheric constituents. Ozone is one of a number of photochemical oxidants in the lower atmosphere that are produced as a consequence of chemical reactions involving sunlight. The formation of ozone (and other atmospheric oxidants) is the result of complex non-linear physical and chemical processes in the atmosphere, including two classes of precursor pollutants: NO_x (nitrogen oxides) and VOC (volatile organic compounds). Thus, in the lower atmosphere, ozone is primarily a secondary pollutant formed from gaseous precursors. Both atmospheric chemistry and meteorological processes have significant roles to play in the formation and transport of ground-level ozone.

2.2 ATMOSPHERIC OXIDANT CHEMISTRY

2.2.1 Sources

The sources of tropospheric ozone are: 1) direct transport from the stratosphere (stratospheric ozone) and 2) photochemical formation from natural and anthropogenic precursors within the lower troposphere. Of these two sources, the latter, is thought to represent the largest source of ground-level ozone (Logan, 1985).

Stratospheric Ozone

In the stratosphere, ozone (O_3) and oxygen (O_2) are part of a natural cycle of formation and destruction that is driven by energy from the sun. Ozone is formed by the photodestruction of oxygen into separate atoms that react with other molecules of oxygen to yield ozone molecules. In turn, the breakdown of ozone and release of molecular oxygen are also triggered by the absorption of UV light. Ozone is distributed throughout the atmosphere, but its concentration varies greatly with altitude. Most of the ozone is concentrated in the middle stratosphere, in a band commonly referred to as "the ozone layer". In the stratosphere, ozone is not a pollutant. Rather it serves a critical function in preventing the penetration of much of the UV light that would otherwise be damaging to life on earth.

There is evidence that some stratospheric ozone is transported down to the free troposphere (Altshuller, 1986; Mukammal et al., 1985; Wakamatsu et al., 1989) contributing to the total ozone observed close to the ground. Under normal conditions, there is little exchange between the lower stratosphere and upper troposphere in mid-latitude regions. However, this situation can dramatically change when deep troughs develop at the tropopause, producing large-scale eddies that carry ozone-rich air parcels downward to the free troposphere. In the northern hemisphere, spring weather conditions appear to favour stratospheric ozone intrusion into the troposphere, coinciding with the periods of highly mobile westerlies. It is estimated that this transport mechanism contributes less than 10 ppb to annual average ground-level ozone (Altshuller, 1986).

Photochemical Ozone Formation in the Troposphere

Tropospheric ozone is formed and destroyed in a series of reactions involving nitrogen oxides (NO_x = nitric oxide (NO) + nitrogen dioxide (NO_2)). Nitric oxide, introduced into the troposphere from various natural and anthropogenic sources, reacts rapidly with ozone to form NO_2 (R1). Nitrogen dioxide absorbs sunlight in the ultraviolet and visible range ($280 \text{ nm} < \lambda < 430 \text{ nm}$) and photodissociates to yield oxygen atoms (O) and NO (R2). The oxygen atoms rapidly combine (time constant $\tau_o \sim 13 \mu s$ (Finlayson-Pitts and Pitts, 1986)) with molecular oxygen (O_2) to produce ozone (R3). The M in R3 represents a third molecule (N_2 or O_2) that absorbs the excess vibrational energy that is released by this reaction and thereby stabilizes the newly formed ozone molecule (Seinfeld, 1986). Reactions R2 and R3 are always the final steps in ozone formation in the troposphere (Warneck, 1988).

Formation and destruction of ozone

$$NO + O_3 \rightarrow NO_2 + O_2 \qquad R1$$
$$NO_2 + h\nu \rightarrow NO + O \qquad R2$$
$$O_2 + O + M \rightarrow O_3 + M \qquad R3$$

In the absence of other chemical species, reactions R1 to R3 govern ozone formation, and a steady state is achieved in which ozone and O are continuously being formed and destroyed (Seinfeld, 1986). Thus, under steady-state conditions, the ozone concentration $[O_3]$ is given by

$$[O_3] = \frac{j_1}{k_1}\frac{[NO_2]}{[NO]} \qquad [1]$$

where k_1 and j_1 are the reaction ($k1 = 26.59 \text{ ppm}^{-1} \text{ min}^{-1}$ at 25 °C) and photolysis ($j_1 \sim 0.533 \text{ min}^{-1}$ during midday in the summer) rate constants for reactions R1 and R2 (Seinfeld, 1986). Several workers have pointed out that measured ozone concentrations are significantly higher than those calculated from [1] in both urban and rural atmospheres (Kelly et al., 1984; Logan, 1985). This shows that the ratio of $[NO_2]/[NO]$ cannot be controlled only by reactions R1-R3; there must be other reactions that convert NO to NO_2 without consuming ozone in situations where ozone concentrations are abnormally high.

The Role of Hydrocarbon Oxidation in Ozone Formation

The atmosphere is never free of chemical species that interfere with the pathway outlined by reactions R1-R3, even in remote locations. In polluted urban atmospheres, elevated levels of hydrocarbons (denoted here as RHs) and NO_x play important roles in ozone formation. Under conditions where hydroxyl radicals can be formed photochemically, hydrocarbons are degraded to produce peroxy radicals ($RO_2^{\bullet}$), which react with NO to produce NO_2 (Atkinson, 1985; Singh, 1987; Warneck, 1988). Therefore, as noted above, these reactions convert NO to NO_2 without destroying ozone. This process can be visualized as follows (other pathways are possible but they are not described here):

Ozone formation (role of hydrocarbon oxidation)

$$\begin{array}{lcll}
RH + HO^{\bullet} & \rightarrow & R^{\bullet} + H_2O & R4 \\
R^{\bullet} + O_2 + M & \rightarrow & RO_2^{\bullet} + M & R5 \\
RO_2^{\bullet} + NO & \rightarrow & RO^{\bullet} + NO_2 & R6 \\
RO^{\bullet} + O_2 & \rightarrow & HO_2^{\bullet} + (RCHO \text{ and/or } R_1R_2CO) & R7 \\
HO_2^{\bullet} + NO & \rightarrow & NO_2 + HO^{\bullet} & R8 \\
2\,(NO_2 + hv) & \rightarrow & 2(NO + O) & R2 \\
2(O + O_2 + M) & \rightarrow & 2(O_3 + M) & R3
\end{array}$$

$$\text{Net:} \quad RH + 4O_2 + hv \rightarrow 2O_3 + H_2O + (RCHO \text{ and/or } R_1R_2CO)$$

A chain of reactions is initiated when RHs react with the hydroxyl radical ($HO^{\bullet}$) (R4) to form water vapour (H_2O) and alkyl radicals ($R^{\bullet}$), which subsequently react with O_2 (R5) to produce alkylperoxy radicals ($RO_2^{\bullet}$). $RO_2^{\bullet}$ in turn reacts with NO (R6) to yield NO_2 and alkoxy radicals ($RO^{\bullet}$), which rapidly combine with O_2 (R7) to produce hydroperoxy radicals ($HO_2^{\bullet}$), aldehydes (RCHO) and/or ketones (R_1R_2CO) (Singh, 1987). The sequence of reactions leading to ozone is completed with R8, R2 and R3, according to which two ozone molecules are formed for each RH molecule converted to RCHO or R_1R_2CO. The well-known observation that ozone concentrations tend to be higher in rural locations downwind of an urban pollution source is consistent with ozone being a secondary pollutant whose formation requires time for the oxidation of hydrocarbons.

In addition to anthropogenic sources, biogenic hydrocarbons emitted by deciduous (isoprene) and coniferous (monoterpenes) forests can act as significant precursors for ozone (Lloyd et al., 1983; Trainer et al., 1987). Biogenic hydrocarbons can significantly affect ozone levels even in urban atmospheres, downwind from emission sources (Chameides, 1988), and their presence can exert a profound influence on the effectiveness of ozone abatement strategies based on curtailed emissions of anthropogenic hydrocarbons and NO_x (U.S. N.R.C., 1991). Measurements and model results at a rural site in central Ontario (Lin et al., 1991) have also demonstrated that natural hydrocarbons, such as isoprene, can significantly contribute to local ozone formation.

The actual situation is more complicated than is implied by Reactions R2 - R8 for two reasons. First, RCHO and R_1R_2CO are themselves substrates for further oxidation, and additional ozone will be generated in each cycle of oxidation until the original hydrocarbons have been completely oxidized to carbon dioxide (CO_2). Considerable work has been done to estimate the overall yield of ozone per molecule of individual precursor hydrocarbons, both anthropogenic and biogenic (Chameides et al., 1992; Carter, 1994; de Leeuw, 1993). The yield of ozone per molecule of precursor is not a straightforward quantity to estimate because it depends on both the amount of the precursor available for oxidation and the rate at which it is attacked by $HO^{\bullet}$. Highly reactive precursors, particularly alkenes, have a strong impact on air quality because their rapid oxidation produces a "pulse" of ozone close to the site of emission.

The second factor is that not all $HO_2^{\bullet}$ radicals produce ozone through the sequence R8, R2, R3, because the ozone-consuming reaction R17 competes for $HO_2^{\bullet}$(see section 2.2.2). The net production of ozone is determined by the relative rates of reactions R8 and R17. In the polluted urban troposphere ("high NO_x" chemistry), the potential for ozone formation is much higher than in remote areas ("low NO_x" chemistry). The mechanism described here explains why both RHs and NO_x are necessary for the occurrence of ozone episodes.

The secondary oxidation of RCHO and R_1R_2CO with $HO^{\bullet}$ can lead both to generation of additional ozone and to other products (Atkinson, 1985), the most important of which (from the pollutant viewpoint) are the alkyl and acyl nitrates, such as peroxyacetyl nitrate (PAN: $CH_3C(O)\text{-}O\text{-}O$). PAN is a noxious compound that is formed by a sequence of reactions from the acetyl radical ($CH_3C(O)^{\bullet} + O_2 \rightarrow CH_3C(O)\text{-}O\text{-}O^{\bullet}$, followed by reaction with $NO_2 \rightarrow CH_3C(O)\text{-}O\text{-}O\text{-}NO_2$). The rate of breakdown of PAN back to $CH_3C(O)\text{-}O\text{-}O^{\bullet}$ and NO_2 is strongly temperature-dependent; it decomposes thermally in the lower troposphere in warm weather with a half-life of a few hours, but is stable for long periods in the upper, colder troposphere (Finlayson-Pitts and Pitts, 1986), where it can be transported long distances.

Sources of Hydroxyl Radicals

The dominant sources of $HO^{\bullet}$ are photochemical; therefore, both its formation and the subsequent formation of ozone are mainly daytime events. The principal route for forming $HO^{\bullet}$ is through the photochemical dissociation of ozone (R9), which produces O_2 and excited oxygen atoms ($O^{\bullet}$); the latter subsequently react with H_2O to form $HO^{\bullet}$ (R10). Photolysis of nitrous acid (HNO_2) to yield NO and $HO^{\bullet}$ (R11) is normally a secondary source of $HO^{\bullet}$, but may sometimes be predominant during the early morning. Photochemical dissociation of RCHO and R_1R_2CO can also lead indirectly to $HO^{\bullet}$ formation. For instance, the photolysis of RCHO produces formyl ($HCO^{\bullet}$) and $R^{\bullet}$ radicals (R12). $R^{\bullet}$ will react with O_2 (R5) to yield $RO_2^{\bullet}$, which produces $HO^{\bullet}$ via reactions R6-R8; $HCO^{\bullet}$ will form carbon monoxide (CO) and $HO_2^{\bullet}$, which also leads to $HO^{\bullet}$ formation (R8). Note that while RCHO and R_1R_2O are emitted into the atmosphere as primary pollutants, they are also produced as secondary pollutants through hydrocarbon oxidation (R4-R8). Their subsequent photolysis causes further ozone production via the pathway R12-R13-R8-R2 and the production of more $HO^{\bullet}$ radicals, which speed up both the overall rate of hydrocarbon oxidation and the formation of ozone.

Hydroxyl radical formation

$O_3 + hv \rightarrow O^{\bullet} + O_2$ R9

$O^{\bullet} + H_2O \rightarrow 2HO^{\bullet}$ R10

$HNO_2 + hv \rightarrow NO + HO^{\bullet}$ R11

$RCHO + hv \rightarrow R^{\bullet} + HCO^{\bullet}$ R12

$R^{\bullet} + O_2 + M \rightarrow RO_2^{\bullet} + M$ R5

$RO_2^{\bullet} + NO \rightarrow RO^{\bullet} + NO_2$ R6

$RO^{\bullet} + O_2 \rightarrow HO_2^{\bullet} + (RCHO \text{ and/or } R_1R_2CO)$ R7

$HCO^{\bullet} + O_2 \rightarrow CO + HO_2^{\bullet}$ R13

$HO_2^{\bullet} + NO \rightarrow NO_2 + HO^{\bullet}$ R8

The major sink for $HO^{\bullet}$ is reaction with NO_2, which leads to the formation of HNO_3 (R14); reaction 15 can become important when NO_2 is low.

Hydroxyl radical sink

$HO^{\bullet} + NO_2 + M \rightarrow HNO_3 + M$ R14

$HO^{\bullet} + HO_2^{\bullet} \rightarrow H_2O$ + Hydroxyl Radical Sink R15

2.2.2 Sinks

Ozone is removed from the troposphere through several processes, including gaseous and aqueous chemical destruction, and deposition at the ground. Of these, it appears that the deposition at the ground dominates the ultimate depletion process (Galbally & Roy, 1980).

Gaseous Chemical Reactions

As a reactive trace component of the atmosphere, ozone can be scavenged by reaction with various free radical (odd electron) species. In polluted atmospheres, the most readily available atmospheric sink for ozone is reaction R1. Reaction R2 does not operate at night and R1 can lead to a complete removal of ozone when sufficient NO is present. In unpolluted atmospheres, NO concentrations are too low to scavenge ozone appreciably. Therefore, nighttime ozone concentrations in rural areas are normally higher than those in urban locales.

Ozone reacts with NO_2 to produce a nitrate radical ($NO_3^{\bullet\bullet}$) and O_2, or NO and O_2 (R18, R19; Singh, 1987). The newly formed $NO_3^{\bullet\bullet}$ can react with NO_2, producing nitrogen pentoxide (N_2O_5), which combines with water to form HNO_3 (R20 and R21). $NO_3^{\bullet\bullet}$ is very rapidly photolysed (to NO_2 and O) and therefore reactions involving $NO_3^{\bullet\bullet}$ are unimportant during daytime (Singh, 1987; Warneck, 1988). On the other hand, $NO_3^{\bullet\bullet}$ is quite reactive and can take over the role of $HO^{\bullet}$ in keeping radical chemistry active when $HO^{\bullet}$ cannot be formed photochemically. Ozone is also reactive with $HO_2^{\bullet}$ and $HO^{\bullet}$ (R16 and R17). These processes are especially important when the NO_x concentrations are low, as in unpolluted atmospheres.

Chemical reactions leading to ozone destruction

$$O_3 + HO^{\bullet} \rightarrow HO_2^{\bullet} + O_2 \qquad R16$$

$$O_3 + HO_2^{\bullet} \rightarrow HO^{\bullet} + 2O_2 \qquad R17$$

$$O_3 + NO_2 \rightarrow NO_3^{\bullet\bullet} + O_2 \qquad R18 \quad \rightarrow \quad NO + 2O_2 \qquad R19$$

$$NO_3^{\bullet\bullet} + NO_2 \rightarrow N_2O_5 \qquad R20$$

$$N_2O_5 + H_2O_{(1)} \rightarrow 2HNO_3 \qquad R21$$

$$O_3 + RH \rightarrow CO + HO_2^{\bullet} + HCHO + \text{other products} \qquad R22$$

In addition to acting as precursors for ozone, unsaturated hydrocarbons also act as sinks. The most important reactions of ozone with tropospheric alkenes are those with ethylene (C_2H_4), propylene (C_3H_6) and butene (C_4H_8) (Henderson et al., 1990; Seinfeld, 1986), as well as biogenic hydrocarbons such as isoprene and monoterpenes (Altshuller, 1983).

Aqueous Chemical Reactions

Ozone can act as an oxidizing agent for several chemical species in solutions (Lelieveld & Crutzen, 1990; Finlayson-Pitts & Pitts, 1986). The importance of these processes is, of course, dependent upon the extent to which the species dissolve in water. Ozone can act as an oxidizing agent for sulphur dioxide (SO_2) in aqueous droplets. In the aqueous phase, SO_2 is converted to bisulphite (HSO_3^-) (R23), which is oxidized by ozone to sulphate anion (SO_4^{2-}) (R24). Modelling indicates that reaction R24 can represent a significant sink for ozone in moist atmospheres rich in SO_2, especially during continuous precipitation. However, the pH of SO_2 solutions is usually less than 5 on account of reaction R23 and, under these conditions, oxidation of SO_2 with H_2O_2 is the predominant pathway for the production of SO_4^{2-} (Schwartz, 1984). Nitrite ion (NO_2^-), which is formed by the dissociation of dissolved HNO_2, can likewise be oxidized to nitrate ion (NO_3^-) by ozone (R28). The importance of reaction R28 as a sink for ozone is small due to low NO_2^- concentrations found in dew, cloud and rain-water (Lee and Schwartz, 1981). However, this mechanism of ozone scavenging could be more important in polluted atmospheres where concentrations of nitrogen compounds are relatively high.

Aqueous phase ozone destruction involving SO_2 or NO_x

$SO_{2(g)} + H_2O_{(l)} \rightarrow H^+ + HSO_3^-$ R23
$HSO_3^- + O_{3(aq)} + OH^- \rightarrow SO_4^{2-} + H_2O + O_{2(aq)}$ R24
$NO_{(g)} + NO_{2(g)} + H_2O_{(l)} \rightarrow 2H^+ + 2NO_2^-$ R25
$2NO_{2(g)} + H_2O_{(l)} \rightarrow 2H^+ + NO_3^- + NO_2^-$ R26

$HNO_{2(g)} + H_2O_{(l)} \rightarrow 2H^+ + OH^- + NO_2^-$ R27

$NO_2^- + O_{3(aq)} \rightarrow NO_3^- + O_{2(aq)}$ R28

The study by Lelieveld and Crutzen (1990) suggests that aqueous phase reactions involving free radicals may destroy ozone directly, and also indirectly decrease the rate of ozone formation by scavenging $HO_2^\bullet$ radicals from the gas phase into water droplets. Some of the dissolved $HO_2^\bullet$ undergoes dissociation to form H^+ and superoxide ions (O_2^-), which rapidly react with ozone and in the process produce OH^- and $HO^\bullet$ (R29 and R30). Thus a cycle of reactions (R29 to R32) is established in which ozone and H_2O_2 are converted to molecular oxygen and water. The intervention of this mechanism (R29 to R32) in moist atmospheres will suppress reaction R8 by inhibiting $HO^\bullet$ formation, thus reducing the rate of ozone formation by reactions R2-R8. Model calculations (Lelieveld & Crutzen, 1990) suggest that in the presence of clouds, tropospheric ozone formation could be decreased by up to 30% through reactions R29 to R32, compared with cloudless conditions.

Aqueous phase ozone destruction involving free radicals

$HO_{2(aq)} \rightarrow H^+ + O_2^-$ R29

$O_2^- + O_{3(aq)} + H_2O_{(l)} \rightarrow OH^- + HO^\bullet + 2O_2$ R30
$OH^- + H^+ \rightarrow H_2O_{(l)}$ R31
$HO^\bullet + H_2O_{2(aq)} \rightarrow HO_{2(aq)} + H_2O_{(l)}$ R32

Net: $O_3 + H_2O_{2(aq)} \rightarrow 2O_{2(aq)} + H_2O_{(l)}$

Ozone Deposition to Vegetation and Other Terrestrial Surfaces

Ozone is readily deposited to vegetation and other terrestrial surfaces in a process known as dry deposition. This process is, to some extent, controlled by the turbulent exchange characteristics of the atmosphere and largely by the properties of the underlying surface (receptors). Taller plant canopies efficiently deplete ozone from the atmosphere (Fowler et al., 1989; Fuentes et al., 1993; Galbally & Roy, 1980; Hosker & Lindberg, 1982) due to the strong turbulent mixing in the overlying air. Turbulent diffusion transports ozone from the free atmosphere to the vicinity of the receptor surface, but surface processes determine the final step in the transfer and uptake mechanism. In the case of foliage, ozone molecules diffuse into the stomatal cavities of leaves, where they rapidly react with compounds present in the membranes of cells beneath these stomatal cavities (Chameides, 1989). There is evidence that the ozone concentration inside stomatal cavities is nearly zero (Amiro & Gillespie, 1985; Chameides, 1989), suggesting that ozone is consumed almost immediately after it arrives at the cell walls of stomatal cavities. Other terrestrial surfaces, such as soil, building structures and water, can also take up and contribute to the removal of O_3 from the lower troposphere (Galbally & Roy 1980; Wesely et al., 1981).

2.3 GROUND LEVEL OZONE PRECURSORS

A brief overview of the physical and chemical characteristics of the precursors NO_x and VOC is provided to give overall context to the formation of ground level ozone. Ambient levels, and the environmental and health effects of the precursors will not be addressed in this assessment.

2.3.1 Nitrogen Oxides

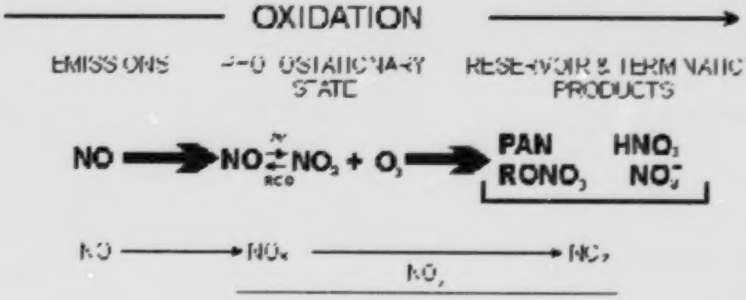
Several chemical symbols (NO_x, NO_y and NO_z) are used to represent the different groups of nitrogen oxide species that are important in the troposphere (Olszyna et al., 1994). These species are determined from measurements of related compounds, as shown in Table 2.2 and Figure 2.1. The family of tropospheric reactive oxidized nitrogen species, generically referred to here as NO_y, is composed of principally NO, NO_2, peroxyacetyl nitrate (PAN), HNO_3 and NO_3-aerosol. Other inorganic and organic species may make additional minor contributions to the total family concentration. These species play several significant roles in tropospheric photochemistry. The primary pollutant, NO, is ultimately oxidized to HNO_3(nitric acid). Removal of nitric acid from the atmosphere by wet and dry deposition constitutes the oxidized nitrogen contribution to acid deposition, which in eastern North America is significant; second to sulphate deposition. Organic peroxy and hydroperoxy radicals are responsible for much of the oxidation of NO to NO_2; hydroxyl radicals oxidize NO_2 to HNO_3 and peroxyacetyl radicals combine with NO_2 to form PAN (see chemistry discussion in Section 2.2). These reactions exert a controlling influence on the radical balance in the troposphere. To the extent that the products are removed from the atmosphere before dissociating, these reactions provide sinks for the radicals and thus also affect the total radical concentration in the troposphere. Since the radicals are responsible for forming the major oxidants of the troposphere (ozone, hydrogen peroxide and organic hydroperoxides), the levels of these oxidants are strongly coupled to the levels of the NO_y

family. The characterization of the levels of these species is therefore essential to the understanding of tropospheric photochemistry.

Table 2.2 Nitrogen Oxides -- Species and Terminology

Formula/Abbreviation	Compound/Definition
NO	Nitric Oxide
NO_2	Nitrogen Dioxide
NO_x	$= NO + NO_2$
PAN	Peroxy Acetyl Nitrate
HNO_3	Nitric Acid
NO_3^-	Particulate Nitrate
RNO_3	Organic Nitrate
HONO	Nitrous Acid
NO_z	$= PAN + HNO_3 + NO_3^- + HONO + RNO_3$
NO_y	$= NO_x + NO_z$

Figure 2. 1 Nitrogen Oxide Species that Participate in Atmospheric Photooxidation (after Olszyna et al. 1994)


OXIDATION
EMISSIONS
PHOTOSTATIONARY STATE
RESERVOIR & TERMINATION PRODUCTS
NO
NO
hν
NO₂ + O₃
PAN
HNO₃
RONO₂
NO₃⁻
NO
NOx
NOy
NOz

2.3.2 *Volatile Organic Compounds (VOC)*

Volatile organic compounds, or VOC, are generally defined as compounds containing at least one carbon atom (excluding carbon dioxide and carbon monoxide) and with a vapour pressure of 0.01 kPa or greater at 25°C. Although there are many thousands of organic compounds in the natural and polluted troposphere that meet the definition of a VOC, most measurement programs have concentrated on the 50 to 150 most abundant C_2 to C_{12} hydrocarbons consisting of the general formula C_xH_y and on C_2 to C_6 carbonyls (compounds that, in addition, contain the structural element :C=O). The categories of VOC most relevant to ground-level ozone formation are summarized in Table 2.3. For this report, total non-methane hydrocarbons (total NMHC) are defined as the sum of all identified C_2 to C_{12} hydrocarbons of formula C_xH_y. Total VOC are defined as total NMHC plus carbonyls. Other categories of VOC, such as halogenated hydrocarbons and methane, are not included in this chapter. Initiated by the presence of sunlight and nitrogen oxides, ozone formation includes a complex array of reactions involving the atmospheric oxidation of VOC. In this process, individual VOC differ in their efficiency towards ozone formation. Therefore, a scale in which each compound is ranked according to its potential to form ozone has long been considered for selective regulation of emissions rather than an approach that treats all VOC equally. Depending on the ranking procedure, different terms have been used to denote the ability of an organic compound to contribute to the formation of ozone. Examples include photochemical ozone-forming potential, incremental reactivity or, simply, reactivity (Paraskevopoulos et al., 1995).

Table 2.3 Important Categories of Volatile Organic Compounds

Category	Example Compounds	Carbon Atoms	Molecular Weight (g/mole)	Propy-Equiv Factor $K_{OH}/K_{OH,Prop}$	MIR[3] (mole O_3/moleC)
Alcohol	Methanol	1	32	0.04	0.37
	Ethanol	2	46	0.12	0.65
Alkane	Ethane	2	30	0.01	0.08
	Propane	3	44	0.04	0.15
	n-Butane	4	58	0.10	0.31
	Hexane	6	86	0.21	0.29
Alkene	Ethylene	2	28	0.32	2.12
	Propylene	3	42	1	2.74
	1-Butene/Isobutene	4	56	1.20	2.10
	trans-2-Pentene	5	70	2.55	2.57
Alkene (Biogenic)	Isoprene	5	68	3.84	2.57
	a-Pinene	10	136	2.03	0.93
Alkyne	Acetylene	2	26	0.03	0.14
Aromatic	Benzene	6	78	0.05	0.11

---

[3] MIR Carter maximum Incremental Reactivity

	Toluene	7	92	0.22	0.74
	m and p-Xylene	8	106	0.77	2.07
Aldehydes	Formaldehyde	1	30	0.37	4.39
	Acetaldehyde	2	45	0.60	2.56
Ketones	Acetone	3	53	0.01	0.21
Ether	Methyl t-Butyl Ether	5	88	0.11	0.23

The species ethylene, m and p-xylene, toluene, propylene and 1,2,4-trimethylbenzene are the most important contributors to reactivity-weighted (using Carter maximum incremental reactivity method [MIR]) total hydrocarbon levels (Table 2.3).

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3 MONITORING TECHNOLOGIES

The information in this chapter is based primarily on that presented in the Report of the Data Analysis Working Group (Multistakeholder NO_x/VOC Science Program, 1997).

The pollutants of interest for assessing ozone pollution are ozone (O_3), nitrogen oxides (NO_x), volatile organic compounds (VOC) and carbon monoxide (CO). In this chapter, only the monitoring of ozone is reported on. For information on the monitoring of the other pollutants, the reader is referred to the aforementioned report, and the Report of the Ambient Air Monitoring Working Group (Multistakeholder NO_x/VOC Science Program, 1997).

3.1 MEASUREMENT METHODS

Measurement of ozone by modern continuous analyzers, many of them portable, became prevalent in the 1970s after the methods outlined below were perfected and routine calibration procedures were developed. The importance of ozone monitoring at frequent intervals had been indicated by apparent effects on vegetation and human health in the 1950s, thereby stimulating the installation of urban monitoring networks. These networks, upon which virtually all of the scientific results in this document are based, are gas analyzers which have short cycle times and store ozone readings each minute, often averaging readings within a 1-hour time step. The specifications for these instruments are presented in Table 3.2. Routine network monitoring of ozone is primarily carried out using continuous gas analyzers that operate on the UV light absorption principle.

Chemiluminescence Method

Chemiluminescence-based analyzers are used at some sites. Light is produced from the energy released in a chemical reaction involving ozone and ethylene. The light emission intensity is proportional to the ozone concentration of the air sampled. The energy generated by the reaction is measured by sensitive photodetectors. Chemiluminescence analyzers are referenced to UV photometric-based transfer standards.

Chemiluminescence reaction:

$$O_3 + C_2H_4 \rightarrow O_2 + C_2H_3OH + hv \text{ (430nm)}$$

An issue with the use of these instruments is the leakage or incomplete burning of the ethylene. Since VOC measurements are necessary at most O_3 monitoring sites the presence of ethylene gas or the products of its incomplete combustion may contaminate these other monitoring systems. Although no other common atmospheric pollutants are known to interfere with these analyzers, water vapour can cause a positive interference and must be corrected for during instrument calibration.

Ultraviolet (UV) Photometry Method

These analyzers are based on the fact that O_3 has a strong absorption band (254nm) which coincides with the emission spectrum from low pressure mercury lamps at 253.7nm. This radiation passes through a chamber (tube) containing ambient air. The light is absorbed by ozone is present in the chamber. The amount of UV light depletion is determined by comparing it with that transmitted through a reference chamber with ozone-free air. The ozone concentration is determined using the Beer-Lambert law. The use of the mercury lamp light source is preferred to burning ethylene for the reasons stated above. The analyzers compare O_3 rich and O_3 stripped air (using MnO_2) and calculate the amount of O_3 present in the original sample air flow. Potential atmospheric interferents include hydrocarbons, mercury vapour, SO_2 and styrene.

UV photolytic reaction:

$$O_3 + hv(253.7nm) \rightarrow O_2 + O$$

3.2 INSTRUMENT PERFORMANCE SPECIFICATIONS

Table 3.1 summarizes the commonly used reference methodologies, measurement principles, and performance specifications for network monitoring. These performance specifications are the NAPS QA/QC (Quality Assurance/Quality Control) guidelines.

Table 3.1 Instrument Performance Specifications for Automated Ambient Air Monitoring Methods for Ozone, NOx, VOC and CO.

Pollutant	Ozone	Met Parameters
Reference Method	Ultraviolet photometry	na
Equivalent Method	Chemi-luminescence	AES protocols
Operating Range	0-1.0 ppm	AES protocols
Minimum Detection Limit	0.005 ppm	na
Noise	0.002 ppm	na
Span Drift -24 hr		
80% of upper range limit	" 5.0%	na
Precision 80% of upper range limit	0.01 ppm	na
Maximum Cycling Time	5 min	1 hour
Averaging Time	1 hour	1 hour

* na - Not Available. Information regarding reference methods and traceability to primary standards can be obtained by contacting Environment Canada's NAPS coordinator.

** Specifications for meteorological measurements are provided in Mar, 1995.

3.3 QUALITY ASSURANCE/QUALITY CONTROL (QA/QC)

3.3.1 Audit Activities and Protocol

The NAPS network has a calibration and audit program to ensure that data reported from the network are high quality (Mar, 1995). Multi-point calibrations are done by the local operating personnel, whereas audits are conducted by personnel who are independent of the day-to-day operation of the station being audited. Audits are conducted at the following levels:

- *Instrument audits* are conducted at random once a year by the operating agency to verify the operational characteristics of the instrumentation.
- *Site audits* are conducted at random once a year by the operating agency to verify the accuracy and validity of the siting criteria.
- *Operational audits* are conducted once a year by the operating agency to verify the appropriate procedures involved with the operation of the site.
- *System audits* are conducted to verify the general operation of the national network, including data validation procedures and should be done by an independent body at least every five years or when the particular agency's operational structure undergoes significant changes.

Presently, the NAPS network has an audit program in place to conduct instrument and site audits on the operating agencies once every two years. Most provincial and municipal agencies within Canada also have some form of audit program. The purpose of the NAPS program is to audit the overall performance of the operating agencies rather than that of individual sites.

3.4 EMERGING TECHNOLOGIES

There is considerable work in progress to improve existing or develop new measurement methods and technologies for monitoring ozone and its precursors. The focus of much of this work has been the refinement of such methods to improve detection limits, better address temporal variability, eliminate interference, and decrease costs. Current resources focus on, but are not limited to: optical remote sensing methods; providing continuous or semi-continuous measurements of VOC; improving NO_x and NO_y speciation and detection limits.

The methodologies for ambient monitoring will continue to evolve as more demands are made to increase the understanding of atmospheric chemistry and monitor a wider range of compounds, with lower detection limits or on a continuous basis. Currently, the following aspects (of routine ozone and ozone precursor monitoring) will benefit from emerging technologies:

- routine measurement of low concentrations of NO_x and CO;
- measurement of speciated VOC and NO_y species by more-sensitive and more-cost-effective means;
- remote-sensing monitoring methods;
- improved telecommunication and data manipulation; and
- interference-free methods for aldehyde measurements.

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4 SOURCES

Ozone is not emitted directly, but is formed as a secondary pollutant through atmospheric chemical reactions with the precursors, NO_x (nitrogen oxides) and VOC (volatile organic compounds). Therefore, the sources and fate of ozone's precursors are an important aspect of understanding ozone concentrations. The data for this section come primarily from the Canadian Emissions Inventory of Criteria Air Contaminants, Environment Canada (1996), and from the Draft Report of the Emissions Inventory Working Group (Multistakeholder NO_x/VOC Science Program, 1997).

The 1990 Canadian Emissions Inventory of Criteria Air Contaminants is currently the most recent data available on emissions of ozone precursors (NO_x and VOC). The 1995 Inventory is in preparation but has not yet been released. The inventory provides national summary data as well as provincial emissions data. The inventory provides emissions estimates for approximately 80 different sector sources, which are condensed into 57 sector sources within five major categories (industrial, transportation, miscellaneous, non-industrial fuel combustion and incineration) in the final inventory report.

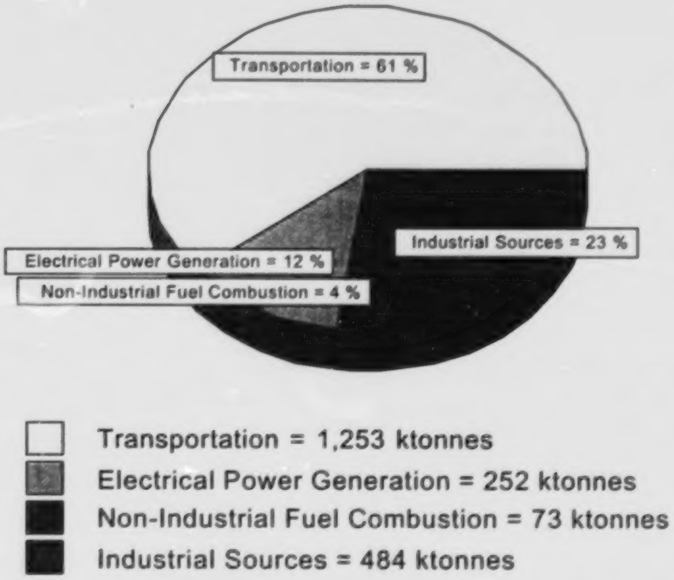
The national emissions inventories are complied by the Pollution Data Branch (PDB) of Environment Canada in collaboration with the provinces and territories. In general, emissions estimates from major industrial sources are compiled by the provinces. The PDB is responsible for compiling data on emissions from the remaining sources, which include anthropogenic and minor industrial sources, the transportation sources, and the fugitive and natural sources.

4.1 NITROGEN OXIDES

Anthropogenic NO_x is the product of stationary and mobile combustion processes. Nitrogen in the fuel source combines with atmospheric oxygen at high temperatures to form several NO_x species of which NO_2 and NO are the most common.

The primary anthropogenic sources of NO_x (Table 4.1) include transportation sources, thermal electrical power plants, and certain industrial processes. Within North America, emissions from the transportation sector and from the electrical utilities plus selected industries account for 98% of total emissions. Within Canada, based upon 1990 emission inventories (Table 4.1), annual NO_x emissions totaled approximately 2.060 million tonnes (2060 ktonnes) with 61% originating from the transportation sector and 23% from the industrial sector. The electric power generating sector produced 12% of national NO_x emissions. (Figure 4.1)

Figure 4.1: 1990 Canadian NO_x emissions by sector (total = 2,060 kilotonnes)



Emissions of NO_x from natural sources account for a small percentage of total emissions. These come from forest fires, lightning and soil microbial activity. The flux of NO_x from the atmosphere to the upper troposphere is very small. Natural NO_x emissions in Canada were estimated at 66kT in 1990, which constituted 3% of the total for anthropogenic and natural sources.

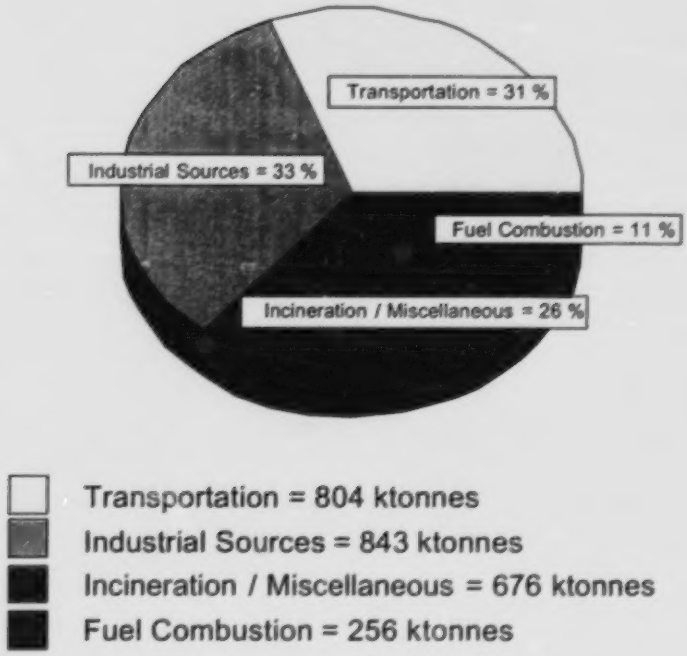
The spatial distribution of NO_x emissions in Canada is shown in Figure 4.3.

4.2 VOLATILE ORGANIC COMPOUNDS

Many hundreds of VOC are included in this category, making generalizations somewhat difficult. VOC are released to the atmosphere by both combustion and evaporation processes. The largest anthropogenic sources of VOC are industrial processes and transportation; other contributors are waste disposal and stationary power plants, compressor stations, etc. Solvent use, petroleum refining and distribution, and chemical manufacturing are the principal industrial sources.

The VOC emission category excludes photochemical non-reactive compounds such as methane, ethane and chloroflurocarbons. In 1990, total Canadian VOC emissions (Table 4.1) were estimated at 2,579 kT (Figure 4.2). The transportation sector produced 31% and the industrial sector 33% of the total emissions. Application of surface coatings, general solvent use and other miscellaneous uses accounted for 24% of VOC emissions. Light duty gasoline car and truck emissions were 22% of the total with 21% produced by upstream oil and gas operations. The distribution of these emissions is shown in Figure 4.4.

Figure 4.2: 1990 Canadian VOC emissions by sector (total = 2,579 kilotonnes)



Biogenic emissions of VOC are mainly from vegetation, usually in the warmer growing season. Isopenes from deciduous forests and monoterpenes from coniferous forests are the important compounds involved in ozone formation.

Biogenic VOC were estimated at 14,644kT in 1990 (Environment Canada 1996) with vegetation contributing 97% of the total. This is about 5.5 times the total anthropogenic contribution of VOC. Within the three ozone problem areas, however, anthropogenic VOC emissions exceed biogenic emissions but biogenic emissions are 2.8 times more reactive than anthropogenic ones. The distribution of biogenic VOC emissions in Canada is shown in Figure 4.5.

Table 4.1 1990 Anthropogenic Emissions of Common Pollutants for Canada

	Emissions in Tonnes	
Category / sector	**NOx**	**VOC**
Industrial Sources		
ABRASIFS MANUFACTURE	214	1,758
ALUMINUM PRODUCTION	3,173	834
ASBESTOS PRODUCTION	895	45
ASPHALT PRODUCTION	260	2,206
BAKERIES	4	3,459
CEMENT AND CONCRETE MANUFACTURE	29,372	186
CLAY PRODUCTS	292	26
COAL INDUSTRY	1,824	2,457
CRUDE OIL PRODUCTION	2,952	4,390
FERROUS FOUNDRIES	30	1,106
GRAIN INDUSTRIES	10	1
IRON AND STEEL PRODUCTION	29,069	27,294
IRON ORE MINING AND BENEFICIATION	6,809	562
MINING AND ROCK QUARRYING	3,243	142
NATURAL GAS PROCESSING	117,489	3,664
NON-FERROUS MINING AND SMELTING	54,594	329
OIL SANDS	15,855	30
OTHER CHEMICALS	15,102	2,818
OTHER PETROLEUM AND COAL PRODUCTS	458	116
PAINT & VARNISH MANUFACTURING	9	1,236
PETROCHEMICAL INDUSTRY	12,990	28,662
PETROLEUM REFINING	33,466	82,264
PLASTICS & SYNTHETIC RESINS FABRICATION	354	12,477
PULP AND PAPER INDUSTRY	61,388	20,165
UPSTREAM OIL & GAS OPERATIONS	3,159	541,874
WOOD INDUSTRY	5,419	15,958
OTHER INDUSTRIES	85,322	88,575
Category total:	**483,751**	**842,636**
Non Industrial Fuel Combustion		
COMMERCIAL FUEL COMBUSTION	24,192	1,055
ELECTRIC POWER GENERATION	252,356	2,280
RESIDENTIAL FUEL COMBUSTION	34,971	2,616
RESIDENTIAL FUEL WOOD COMBUSTION	5,462	250,526
Category total:	**316,982**	**256,478**

Table 4.1 cont. 1990 Anthropogenic Emissions of Common Pollutants for Canada

	Emissions in Tonnes	
Category / sector	**NOx**	**VOC**
Transportation		
AIRCRAFT	18,506	7,252
HEAVY-DUTY DIESEL VEHICLES	324,277	36,555
HEAVY-DUTY GASOLINE TRUCKS	11,943	11,445
LIGHT DUTY GASOLINE TRUCKS	95,323	137,294
LIGHT DUTY GASOLINE VEHICLES	294,501	441,800
LIGHT-DUTY DIESEL TRUCKS	2,610	1,088
LIGHT-DUTY DIESEL VEHICLES	1,959	679
MARINE	47,346	32,174
MOTOR CYCLES	540	3,023
OFF-ROAD USE OF DIESEL	271,643	27,763
OFF-ROAD USE OF GASOLINE	47,153	95,747
PROPANE POWERED VEHICLES	2,803	1,674
RAILROADS	134,143	6,599
TIRE WEAR	0	815
Category total:	**1,252,748**	**803,908**
Incineration		
OTHER INCINERATION	2659	2594
WOOD WASTE INCINERATION	4882	52898
Category total:	**7,541**	**55,492**
Miscellaneous		
APPLICATION OF SURFACE COATINGS	4	177,520
CIGARETTE SMOKING	0	0
DRY CLEANING	1	11,985
FUEL MARKETING	0	96,654
GENERAL SOLVENT USE	9	289,888
MARINE CARGO HANDLING INDUSTRY	0	1
PESTICIDES AND FERTILIZER APPLICATION	746	42,113
STRUCTURAL FIRES	514	2,376
Category total:	**1,275**	**620,538**
TOTAL FOR CANADA	**2,062,297**	**2,579,051**

* The Carbon Black Sector was grouped under the Other Industries Sector to protect the confidentiality of the information.

Figure 4.3 Distribution of 1990 annual NOx emissions in Canada

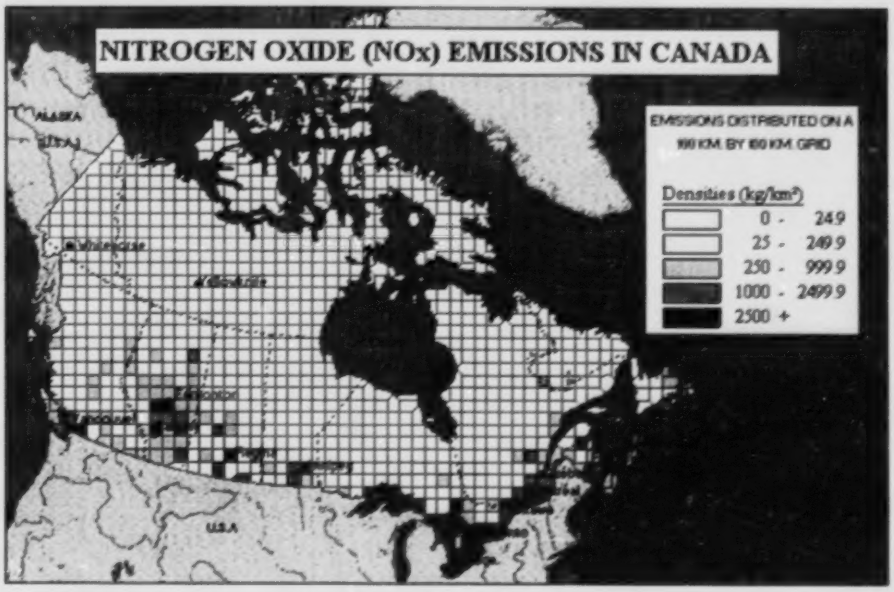

NITROGEN OXIDE (NOx) EMISSIONS IN CANADA
EMISSIONS DISTRIBUTED ON A 100 KM BY 100 KM GRID
Densities (kg/km²)
0 - 24.9
25 - 249.9
250 - 999.9
1000 - 2499.9
2500 +
ALASKA
(U.S.A.)
Whitehorse
Yellowknife
Edmonton
Vancouver
U.S.A.

Figure 4.4 Distribution of 1990 anthropogenic VOC emissions in Canada

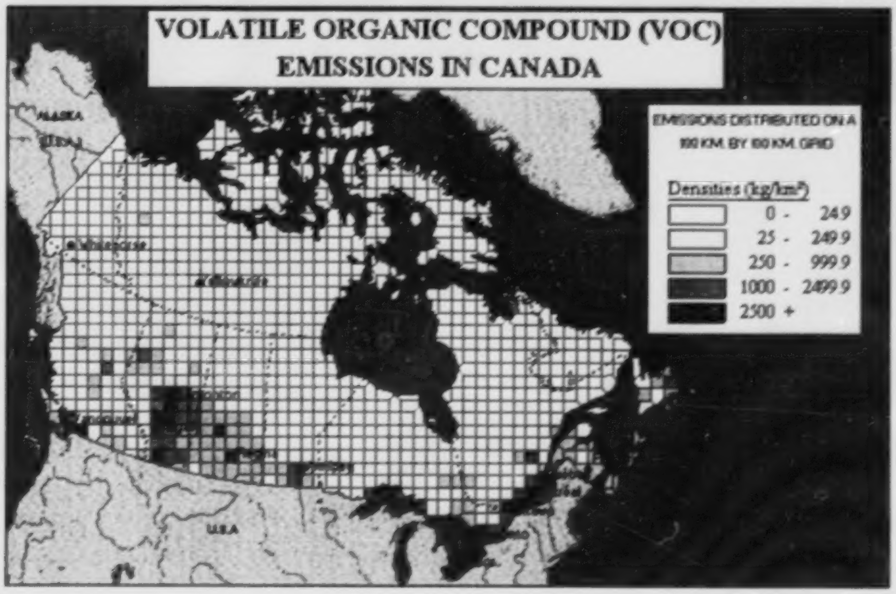
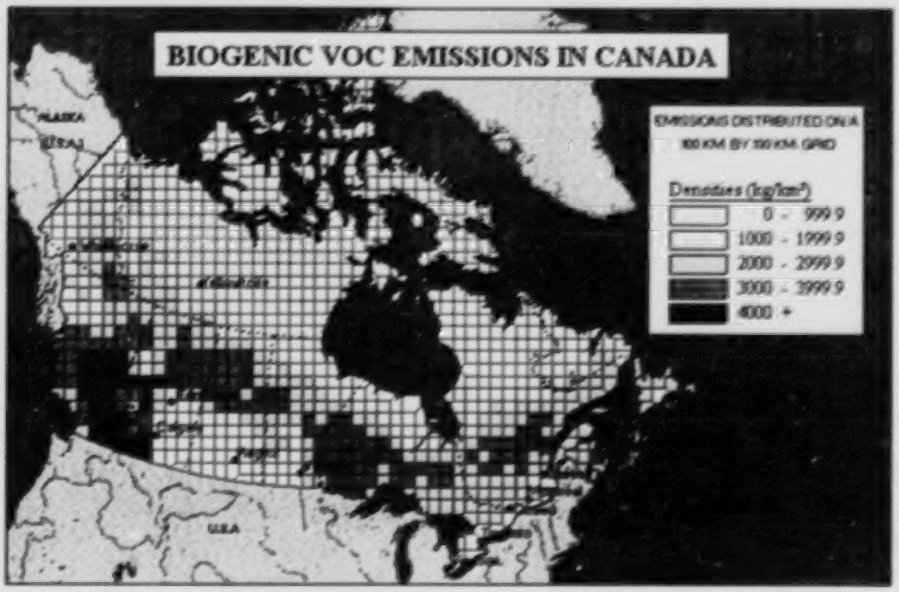

VOLATILE ORGANIC COMPOUND (VOC) EMISSIONS IN CANADA
EMISSIONS DISTRIBUTED ON A 100 KM BY 100 KM GRID
Densities (kg/km²)
0 - 24.9
25 - 249.9
250 - 999.9
1000 - 2499.9
2500 +
ALASKA
(U.S.A.)
Whitehorse
Yellowknife
Edmonton
Vancouver
U.S.A.

Figure 4.5 Distribution of 1990 biogenic VOC emissions in Canada


BIOGENIC VOC EMISSIONS IN CANADA
ALASKA
EMISSIONS DISTRIBUTED ON A
100 KM BY 100 KM GRID
Densities (kg/km²)
0 - 999.9
1000 - 1999.9
2000 - 2999.9
3000 - 3999.9
4000 +
U.S.A.

4.3 UNCERTAINTIES IN EMISSIONS INVENTORIES

Emission inventory reporting in Canada is voluntary in most provinces with statistics for larger single sources being more accurate than smaller, more widely distributed sources. Estimates of overall accuracy suggest a ±20% range of uncertainty for NO_x. VOC information is less accurate that that for NO_x, however, the overall proportion of sources provides a general pattern that should be confirmed for any area which requires closer study. The 1995 Environment Canada inventory is expected to be more accurate than the figures presented here.

REFERENCES

Environment Canada (1996). Canadian Emissions Inventory of Criteria Air Contaminants (1990). Report EPS 5/AP/7E; 75p.

Multistakeholder NO_x/VOC Science Program, (1997). Draft Report of the Emissions Inventory Working Group.

Health Canada	Santé Canada

Environment Canada	Environnement Canada

NATIONAL AMBIENT AIR QUALITY OBJECTIVES FOR GROUND-LEVEL OZONE

SCIENCE ASSESSMENT DOCUMENT

A Report by
the Federal-Provincial Working Group
on Air Quality Objectives
and Guidelines

July, 1999

This document has been divided into a series of files for easier downloading from our web site.

Part 2 of 7

Canada

5 ENVIRONMENTAL LEVELS

The information in this chapter is based primarily on that presented in the Report of the Data Analysis Working Group (Multistakeholder NO_x/VOC Science Program, 1997).

This chapter provides information on ambient levels of ground-level ozone and the climatic conditions contributing to elevated ozone levels in different areas of Canada. The chapter begins with a discussion of background ozone concentrations. Ambient ozone data are then analyzed to explore seasonal, diurnal and weekday-weekend patterns in ozone levels, as well as long term trends. These analyses are all based on 1 hour ozone data. The chapter concludes with a discussion of ozone data for an 8 hour averaging period and an analysis of the relationship between 1 hour and 8 hour data is presented.

For a more comprehensive treatment of ozone concentrations and discussion of the factors affecting these, readers should consult the Report of the Data Analysis Working Group: Ground Level Ozone and Its Precursors, 1980-1993 (Multistakeholder NO_x/VOC Science Program, 1997). This same report should also be consulted for information on ambient levels of NO_x and VOC in Canada.

5.1 BACKGROUND OZONE CONCENTRATIONS

Ozone concentrations at remote rural sites are measured in order to estimate background levels in the absence of (significant) anthropogenic ozone. Background ozone at remote sites is a product of natural sources of the gaseous precursors, long range transport of ozone, and contributions from stratospheric intrusion. The natural background level of ozone at remote sites provides a lower limit target for ozone reduction through the control of anthropogenic nitrogen oxide (NO_x) and volatile organic compound (VOC) emissions.

5.1.1 Literature Review

A review of the literature provided estimates of background ozone concentrations for a number of countries in both the northern and southern hemisphere.

Background concentrations are estimated from sites considered to be representative of the well-mixed boundary layer. Several parameters were considered in selecting sites which could provide appropriate data. Broadly taken, the characteristics of the selected sites were that they should be remote from anthropogenic sources, exhibit minimal diurnal variation, be representative of continental air masses, and be representative of the free troposphere.

There are two general characteristics of ozone concentrations at remote sites. First, they generally exhibit diurnal trends of less than about 5 ppb. Second, the highest ozone concentrations occur in late winter or early spring. The literature review indicates that, based on comparisons of current concentrations with those estimated for the late 1800s, there are no locations truly unaffected by anthropogenic ozone. One possible exception is American Samoa, which currently has the lowest observed ozone level in the world (Oltmann & Levy, 1994; Oltmann & Komhyr, 1986). It has been proposed that anthropogenic activities have resulted in an increase in surface ozone concentrations which are estimated globally to be two to four times greater than pre-industrial levels (Bozo & Weidinger, 1995; Cartalis & Varotsos 1994; Altshuller, 1987; Bojkov, 1986; Singh, et al. 1978). Historical data and modelled estimates of average daytime ozone concentrations under conditions not affected by anthropogenic emissions give a range of 10-20 ppb.

Given the prevalence of anthropogenic sources of precursor emissions and the near-complete mixing throughout the boundary layer, the origin of sampled air masses ought to be considered, (e.g. by using trajectory analysis). Unfortunately, very little of the ozone from remote sites is reported with the necessary concurrent meteorological information.

Literature Estimates of Daily Maximum One Hour Ozone Concentrations

Table 5.1. provides estimates of average daily maximum ozone concentrations (for all months). Not all studies accounted for the occasional impact of polluted air masses, thus the ranges reported occasionally extend to greater than 50 or 60 ppb. For example, the estimate for the western United States summertime daily maxima range is from 50 to 78 ppb, which is indicative of the infrequent impact of polluted air masses from anthropogenic source regions or isolated events such as forest fires (Altshuller & Lefohn, 1996). The range of reported daily maximum ozone for continental air masses in the northern hemisphere is 30 to 60 ppb. Estimates of daily maximum concentrations, from studies using trajectory analysis to identify the least affected remote sites, fall at the lower end of the range, 30 to 40 ppb. Higher concentrations may be observed during late spring or early summer due to stratospheric intrusion.

Table 5.1 Average Daily Maximum Ozone Concentrations in the Northern Hemisphere

Reference	**Location**	**Range of Daily Maximum Hourly Ozone (ppb)**
Angle and Sandhu, 1986	Northern Alberta, Canada	27 - 66
Altshuller and Lefohn, 1996	Western U.S., summertime	50 - 78
Colbeck and Harrison, 1985	Stodday, UK	41.5 - 50.6
Evans et al., 1983	U.S. National Forests	33 - 49
Kelly et al., 1982	South Dakota, U.S.	34 - 36
Legge et al., 1991	Rocky Mountains, Alberta, Canada	64.2
Singh et al., 1978	Continental U.S.	17 - 75
	Hawaii, U.S.	30 - 59
	Germany	18 - 52

Estimates of Average Monthly Concentrations

For data records greater than one year, the average of the monthly means is often reported to evaluate seasonal differences in ozone concentrations. Higher values are typically found in the late winter through early spring months. Monthly means from a number of remote sites have been shown to fall in the range of approximately 20 to 45 ppb. Higher values are observed at high elevation sites.

A spring through early summer ozone maximum was observed at many rural and remote sites in the Northern Hemisphere mid-latitudes in the late 1850s to early 1900s (Lisac & Grubisic, 1991; Feister & Warmbt, 1987; Mukammal et al., 1985; Meagher et al., 1987). In the 1980s and 1990s, the spring maximum has also been observed at a number of remote sites (Angle & Sandhu, 1989; Meagher et al., 1987; Scheel et al., 1990; Singh et al., 1978). However, at some remote sites, a summer maximum is becoming more evident as a result of an increase in the importance of photochemical production of ozone from precursor emissions (Hough & Derwent, 1990). The spring maximum is believed to be influenced by the annual cycle of stratospheric ozone production and stratospheric intrusion (Junge, 1962; Logan, 1985). Although at some sites, the relative importance of stratospheric/tropospheric processes versus photochemistry is decreasing (Follows & Austin, 1992) or small (Altshuller, 1987; Liu et al., 1987; Fabian & Pruchniewicz, 1976), there are other sites where seasonal and regional differences of stratospheric/tropospheric processes can strongly influence ozone concentrations (Penkett & Brice, 1986). The yearly mean flux of stratospheric ozone is highest between 30°N to 60°N latitudes (Singh et al., 1978; Fabian and Pruchniewicz, 1976). Altshuller (1987) concluded that average spring through summer background ozone contributions from stratospheric intrusion or upper tropospheric ozone were <10 ppb, while other studies suggest that stratospheric contributions to high ozone levels can be significant (Wakamatsu et al., 1989; Derwent et al., 1978).

A short study to estimate the contribution of stratospheric ozone to surface-measured ozone was carried out during February to May, 1992, at Mt. Tremblant in Québec (Besner et al., 1994). This limited study indicated that the stratospheric ozone contribution to surface ozone was about 6 to 20%. However, contrary to expectations, the lowest percentages were associated with meteorological conditions considered most conducive to stratospheric input (specifically, passages of cold fronts). In reviewing the many studies on stratospheric contribution to tropospheric surface ozone, the conclusions are fraught with large uncertainties and the results are as yet inconclusive.

Summer Season

Given the ubiquitous impact of anthropogenic emissions in the well-mixed boundary layer, it is relevant to assess background concentrations during the summer when photochemical production of ozone is most significant. The range of monthly averages for the period May through September is approximately 25 to 45 ppb. Since the spring maximum usually occurs in April to early June, and the seasonal minimum in September to November, this range in summer concentrations reflects the entire seasonal range (see above), especially in very clean areas where the seasonal amplitude is small.

Estimates of Annual Averages

The annual average hourly ozone concentrations at remote sites is typically higher than at anthropogenically influenced sites, given the strong influence of precursor emissions on the diurnal pattern of the latter. In urban areas, ozone concentrations often fall to near zero at night due to titration by NO (see section 5.3.2 for more detail). For example, the 1989 annual average at Jardin Botanique, Montréal, was 17.0 ppb with a standard deviation of 16.6. For the same year, Montmorency, a forested site north of Québec City, had an annual average of 32.9 ppb with a standard deviation of 10.8.

5.1.2 Ozone Concentrations at Remote and Rural Sites in Canada

Fifteen Canadian sites (Figure 5.1) have been identified as characteristic of regions with little anthropogenic influence that have the potential to provide estimates of background ozone levels in Canada. Not all the sites are currently in operation. The relevant metrics of the ozone concentrations at these sites are presented in Table 5.2. These statistics were selected as being indicative of the behaviour of ozone in remote areas, i.e., low daily maximum concentrations and minimal seasonal amplitude in average monthly concentrations, with highest monthly averages observed in early spring (April and May).

The typical range of monthly average concentrations observed at remote sites in Canada is 20 to 40 ppb (Column 7 Table 5.2), with 12 month average daily maxima from about 30 to 40 ppb. Typical average daily maxima are higher for the summer period (May through September) and are in the range from 35 to 50 ppb (Column 6 Table 5.2 and graphically in Figure 5.2). This illustrates the impact of higher concentrations in the spring, which occasionally extend into May, and the impact of photochemical reactions, which are more prevalent in the warmer summer months.

Those sites marked with an asterix (*) in Table 5.2, that show higher average annual maxima (in Nova Scotia, southern Québec and central Ontario), are affected by anthropogenic emissions due to long-range transport. To truly characterize the background ozone concentrations at these site would require a detailed wind or trajectory analysis.

The ozone at these remote and rural sites is influenced by elevation and mountain top sites generally exhibit higher concentrations. These higher elevation sites may be within the free troposphere and more frequently affected by stratospheric intrusion, as described in the previous section. Typically, sites above 850m experience higher ozone concentrations (Lefohn et al.1990a; Wolff et al. 1987).

Figure 5.1 Rural and Remote Sites in Canada

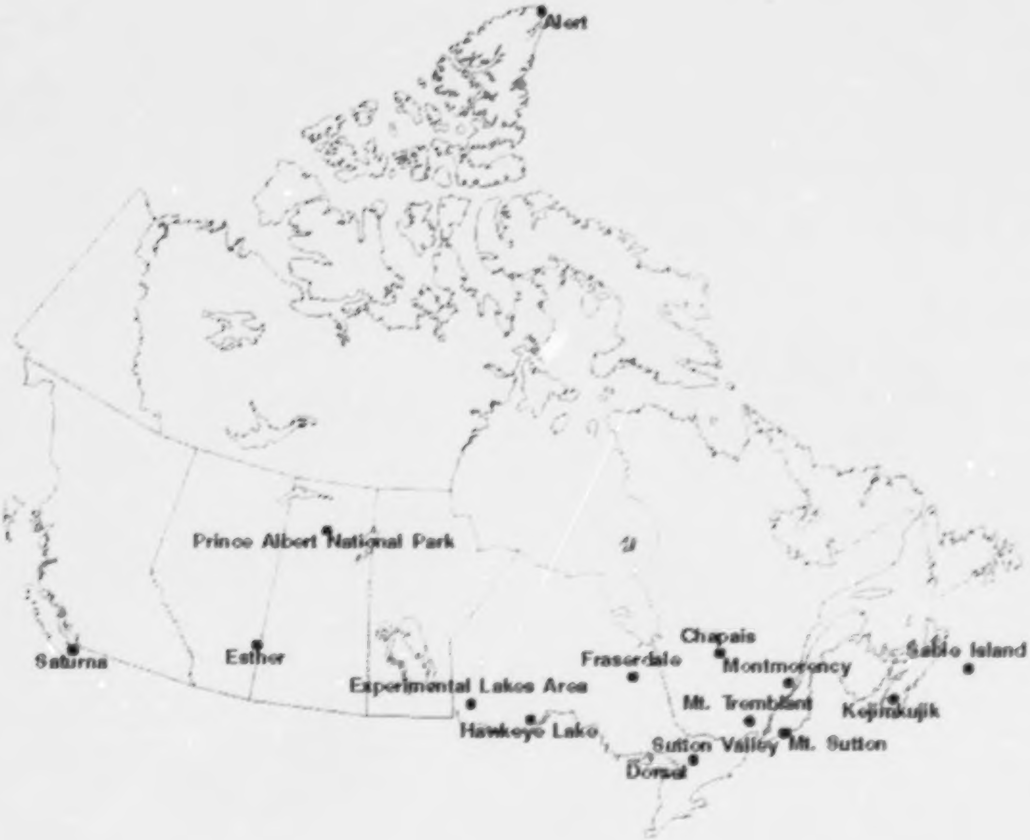

Alert
Prince Albert National Park
Saturna
Esther
Experimental Lakes Area
Hawkeye Lake
Fraserdale
Chapais
Montmorency
Sable Island
Mt. Tremblant
Kejimkujik
Sutton Valley
Mt. Sutton
Dorset

Table 5.2 Summary Statistics for Canadian Remote and Rural Sites

Site	Data Record (Avg. Period)	Elevation	Average of Annual Max.[1]	Average for Data Record[2]	Range of Average Daily Max. (May - Sept.)[3]	Range of Monthly Average[4] (All Months)
Alert, N.W.T.	1/92 - 12/94	210m	47.3	28	24 - 27	16 - 35
Sable Island, NS*	1/92 - 12/94	4m	129.3	34	39 - 45	27 - 47
Kejimkujik, NS*	4/85 - 12/92	155m	100.3	27	37 - 47	20 - 34
Mt. Tremblant, Que.*°	1/87 - 12/94	860m	107.6	34.8	46 - 54	28 - 45
Mt. Sutton, Que.*°	1/87 - 12/94	845m	100.0	36.9	49 - 58	28 - 46
Sutton Valley, Que.*	1/87 - 12/94	250m	86.6	29.7	41 - 49	24 - 39
Montmorency, Que.	5/88 - 12/92	790m	92.0	29	37 - 45	25 - 35
Chapais, Que.	6/88 - 12/90	381m	82.7	27	40 - 41	18 - 35
Dorset, ON*	4/81 - 12/91	na	100.5	28	41 - 55	21 - 34
Fraserdale, ON	3/90 - 12/94	205m	80.7	28	35 - 39	22 - 37
Hawkeye Lake, ON	6/83 - 12/91	na	76.0	27	36 - 48	21 - 38
ELA, ON	5/88 - 12/92	369m	73.3	33	37 - 43	26 - 40
Prince Albert NP, SK	2/94 - 09/94	na	57	~25	~30	22 - 39
Esther, AB	7/94 - 9/95	707m	64.0	28	45 - 45	18 - 34
Saturna, BC*	5/91 - 12/92	178m	65.0	25	38 - 41	

[1] Average of the maximum hourly ozone concentrations observed each year over the entire data record.

[2] Average of all hourly ozone concentrations observed for the entire data record.

[3] Range in average of daily one-hour maximum ozone concentrations for May-Sept. computed for each year.

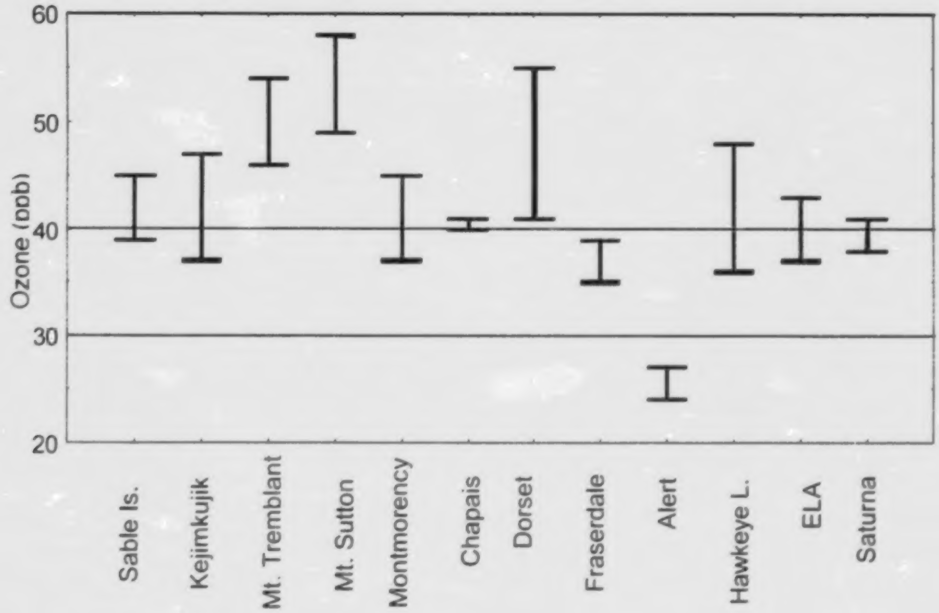
[4] Range of monthly average ozone concentrations, averaged over entire data record.

* indicates sites affected by long-range transport of anthropogenic emissions

° indicates mountain-top sites

Alert, NWT may be considered as the only truly remote site at which ozone data are currently available in Canada. There are no anthropogenic sources nearby, nor is it located within major atmospheric transport corridors which could carry anthropogenic emissions to it. Another continental site with the potential to experience clean air masses is Fraserdale, Ontario.

Figure 5.2 Yearly variation in Mean Daily Maximum Hourly Ozone Concentrations (May to September) for Selected Remote and Rural Sites



5.1.3 *Summary*

Background ozone concentrations vary seasonally and geographically; thus it is not possible to identify a single value for background ozone concentrations. The ozone concentrations observed at remote sites in Canada are similar to those reported for other locations in the Northern Hemisphere (Lefohn et al. 1990b). Reasonable estimates for the range of ozone concentrations at rural remote Canadian surface sites, and typical of the Northern Hemisphere, are:

• Average daily 1-hr. maxima (all months)	30 - 48 ppb
• Average daily 1-hr. maxima (May - Sept.)	35 - 48 ppb
• Monthly 1-hr. average (May - Sept.)	25 - 40 ppb

5.2 GEOGRAPHIC AND METEOROLOGICAL FACTORS AFFECTING OZONE IN CANADA

An overview of the impact of local meteorology and long-range transport is presented below, followed by a more detailed description of the geographic and meteorological factors contributing to ambient ozone levels in different regions of Canada.

5.2.1 Local Meteorology

Meteorological processes play a significant role in the movement of ozone and its precursors. High ozone episodes are often associated with slow moving, high pressure weather systems which concentrate pollutants and provide the higher temperatures and solar radiation that enhance ozone formation. These weather systems are characterized by sinking of air through much of the troposphere, which has the effect of trapping localized pollutants and preventing their dilution through convective mixing into the upper troposphere.

Temperature inversions associated with these events are experienced in all parts of Canada, but are especially significant in the Lower Fraser Valley region of B.C. where adjacent mountains act to further confine the air mass. With high pressure weather systems, surface winds are typically light, prompting the accumulation of pollutants near the ground. These effects are most pronounced close to the summer solstice (May-September) when ambient temperatures, sun angles and day length favour ozone formation. With the passage of cold air, the high pressure ridge breaks down permitting the entry of cooler, cleaner air and the subsequent mixing of ambient pollutants.

5.2.2 Long-Range Transport

Establishing the distinction between ozone generated locally and that occurring as a result of advection by winds into a region (known as long-range transport or LRT) is vital to understanding and controlling ambient ozone levels. Previous studies in the Windsor-Québec City corridor (Yap et al., 1988) and the Southern Atlantic region (Thorburn, 1981), have estimated that long-range transport from the United States often accounts for a significant percentage of the ozone and its precursors (NO_x and VOC) observed in these regions during episode conditions.

Ozone and its precursors can be transported over distances that range from hundreds to a few thousand kilometres. Before finally arriving at a receptor site, the pollutants entrained in the air mass may traverse several source areas, change pathways, undergo chemical changes, or experience depletion by dry deposition. Consequently, the task of identifying the contribution of local versus more distant sources is difficult, and is particularly so in areas with multiple sources of oxidants.

Source identification (local and long-range), and quantification of source strength, in situations involving multiple sources that are spread over a broad geographic region with varied emission characteristics, is done with three dimensional air quality emission based modelling. Current modelling results are discussed in the reports of the Lower Fraser Valley Modelling and Measurement Group and the Windsor-Québec City Corridor and Southern Atlantic Region Modelling and Measurement Group (Multistakeholder NO_x/VOC Science Program, 1997).

5.2.3 The Lower Fraser Valley, B.C.

This area extends from the Strait of Georgia in the west to the Fraser Canyon in the east. The valley is bound by the Coast Mountains to the north and the Cascade Range to the southeast. The population of British Columbia is highly concentrated in this lower mainland area, especially within the Greater Vancouver Regional District (with approximately 1.5 million people). Consequently, most anthropogenic emissions for the province originate here, principally, from motor vehicles and, to a lesser extent, from stationary sources, such as commercial and industrial fuel combustion, gasoline refining and retailing (Robeson & Steyn, 1990). Unlike the Windsor–Québec City corridor and the Southern Atlantic region, where significant levels of pollutants can be advected from distant sources, both ground-level ozone and precursors originate primarily in the Lower Fraser region. However, in the eastern part of the valley, NO_x, VOC and ozone can be transported from the state of Washington under appropriate meteorological conditions.

When compared with other urban areas in Canada, precursor emission rates in the Lower Fraser Valley are not especially significant (Canadian Council of Ministers of the Environment (CCME), 1990), but the geographic features of this area can produce high ozone concentrations during synoptic conditions that feature light winds and poor dispersion. Concentrations can also vary spatially within this area. At the eastern end of the Burrard Inlet, the maximum one-hour concentration in any given year averages about 100 ppb, while in the western section of Greater Vancouver District and south Vancouver, ozone levels seldom exceed 82 ppb. Bounded on the west by the waters of the Strait of Georgia and the Pacific Ocean, and with the west-facing mountains to the east, the Lower Fraser Valley experiences light winds, predominantly from the northwest in summer, and frequent easterly flows. Under strong solar radiation input, differential heating between the land and water produces sea breezes, which are quite common in summer. The cool marine air helps to moderate the temperature over the land, but, at the same time, it limits the mixing depth of the polluted air. Further, under stagnant anticyclonic conditions with light wind, the mountains act as barriers to pollutants emitted within the Lower Fraser region, channeling them instead along the valley, which ultimately leads to high levels of ozone and its precursors near the ground.

5.2.4 Alberta, Saskatchewan and Manitoba

The Prairie Region includes Alberta, Saskatchewan and Manitoba. Although this area is denoted as the prairie region, it includes the mountain range and rolling foothills in western Alberta, and the Canadian Shield of northern Saskatchewan and Manitoba. This region lies between the 49th and 60th parallels of the latitude, which places it in the central belt of the northern cool temperate zone. The climate is characterized by long, cold winters, and short, warm summers. Prevailing upper level winds are west-northwest. Because mechanisms governing ozone concentrations are dependent upon climatic variables such as temperature, solar radiation and surface albedo, ozone concentrations measured in the region exhibit different characteristics from those measured in more moderate, southerly climates. Throughout this region, there is a wide range of NO_x and VOC sources, including large industrial point sources, small to medium cities with populations less than three quarters of a million, and extensive areas of biogenic emissions.

Rural long-term averaged ozone concentration is relatively high when compared with those in cities or more southerly locations. Tropopause folding introduces stratospheric ozone into the troposphere where a variety of transport processes move it further downward. Boundary-layer mixing then delivers this ozone to the surface. Stratospheric intrusion, which is the direct injection of extremely high concentrations of ozone to the surface, seems to be rare with only one incident reported in Regina, Saskatchewan. Photochemical reactions with naturally emitted ozone precursors also contribute to rural ozone concentrations.

Background ozone transported from rural locations is largely responsible for episodes of high ozone concentrations at urban stations. However, exceedances of the current 1 hour ozone objective are infrequent, only a few hours per year in larger cities. These exceedances generally occur under hot stagnant weather conditions when photochemical reactions involving anthropogenic emissions can add to the background ozone.

5.2.5 The Windsor–Québec City Corridor

This area, located in the broad geographic region known as the Great Lakes–St. Lawrence Lowlands, is the population and industrial heartland of Canada. It holds almost 60% of Canada's population, produces about 70% of the value of manufactured goods, and has the highest densities of people, agriculture and economic activities in Canada. This corridor also has about half of Canada's large and medium-sized cities, including two of the largest metropolitan areas in Toronto and Montréal. In this area, the principal anthropogenic sources of precursor emissions are from the transportation sector, thermal power plants and a wide range of industrial sources. However, the region lies in the path of major air streams, which are responsible for a significant percentage of pollutants being transported into this area from U.S. sources. The most dominant path follows a northeasterly course through southern Ontario, up through the St. Lawrence River Valley and out to the North Atlantic.

Ozone episodes are more frequent and of longer duration than those in other parts of Canada. This is partly attributed to the usually longer and warmer summers, and frequent anticyclonic (high pressure) conditions. The region has a continental climate, although, in central and western southern Ontario, it is markedly modified by the Great Lakes. The southwestern region of Ontario experiences the longest and warmest summers, averaging 20°C. Temperatures in the large urban areas can be up to 5°C higher than the surrounding countryside, although in Toronto, the opposite effect can occur near the shore of Lake Ontario. The weakest winds occur in the summer and blow predominantly from the southwest.

5.2.6 The Southern Atlantic Region

The topography of this area is typified by rolling hills, mostly below 300 metres in elevation. Forest cover, consisting of mixed evergreen and deciduous species, is extensive. During the ozone season, this region is strongly influenced by air streams from the south and southwest that have travelled from central Canada along the St. Lawrence River Valley, or along the Atlantic seaboard, often crossing the northeastern United States. The majority of episodes of high ozone in the Southern Atlantic region are associated with the long-range transport of pollutants along one of these trajectories. During the fall, winter and early spring, winds blow predominantly from the west and the northwest (e.g. Arctic air flows).

The two regions that experience the highest ozone levels (maximum one-hour concentrations ranging from 90-110 ppb) are western Nova Scotia and southern New Brunswick. However, it should be noted that there are no monitoring sites in northern New Brunswick or eastern Nova Scotia. Based on an examination of all available data, including that from a site on Prince Edward Island, the potential for high hourly ozone concentrations probably exists throughout New Brunswick and Nova Scotia.

Significant metropolitan centres in the Atlantic region include Saint John and Moncton, New Brunswick, with populations of about 125,000 and 102,000, respectively, and Halifax, Nova Scotia, with 320,500 people (1991 census data). Mobile sources contribute to NO_x and VOC emissions in all these centres; both Halifax and Saint John also have power plants and oil refineries, which are significant local sources of NO_x and VOC. There are some additional point sources within the region outside the urban centres, including power plants and pulp and paper mills.

5.2.7 Summary

Both meteorological processes and geographic/topographic features are important factors affecting ambient ozone levels. The meteorological conditions that are necessary for the occurrence of high ozone concentrations are well documented; they involve slow moving, anticyclonic (high pressure) weather systems. These systems, characterized by slow wind speeds, and sinking of air through the troposphere, are conducive to trapping air pollutants near ground level and preventing their dispersion and dilution. Since ground level ozone is a photochemical pollutant, the formation of ozone is maximal over the summer season (May-September), when higher ambient temperatures, more intense solar radiation and longer day lengths favour greater photochemistry. Therefore, ozone episodes are generally associated with climatic and meteorological conditions that lead to both enhanced ozone production and limited dilution/dispersion. Geographic and/or topographic features of a region can exacerbate this situation by affecting either of these processes.

In addition to these factors, some regions of Canada, namely the Windsor-Québec Corridor and the Southern Atlantic Region, are affected by the long range transport of ozone and its precursors from source regions, both within Canada and the United States.

5.3 OZONE CLIMATOLOGY

Ambient monitoring of ozone is performed throughout Canada under the National Air Pollution Surveillance (NAPS) network, a collaboration of federal, provincial and municipal monitoring agencies. There were 153 Canadian ozone monitoring stations reporting data from 1986-93. Of these sites, 112 were located in urban or suburban areas and 41 in rural locales. As discussed in Section 5.1.2, few sites with long-term data sets were located in remote rural locations.

Ozone data were analyzed to illustrate seasonal, diurnal and day-of-the-week patterns in ozone levels. A detailed analysis of all sites in Canada was conducted (Fuentes and Dann, 1993), and only sites representative of different land use (urban, suburban, rural, rural-remote) and different geographical regions are featured here. Most figures deal with the 1986-93 time period and include only the months of May to September. The focus on the "summer" season reflects the months with elevated photochemical ozone, and on the time of year when primary receptors (humans and vegetation) are most at risk due to greater exposure to ambient ozone.

Generally, only sites with more than 75% data capture were used: however, because of a scarcity of monitoring sites in some areas, sites are shown that were not operational in all years between 1986 and 1993. Monitoring at many of the non-urban sites was carried out as part of specific research programs and the data have not been provided to the National Air Pollution Surveillance (NAPS) archive. The province of Québec has operated an extensive rural ozone monitoring network of 16 sites since 1989, but currently data for only five Québec rural sites are in the NAPS database.

Ozone concentration percentiles (5, 10, 25, 50, 75, 90, 95, 98, 99, 99.9), and mean and standard deviation values were calculated for selected stations representative of most cities and regions, as shown in Table 5.3. These ozone statistics are provided for all data between 1986 and 1993 (May to September). Ozone data for several stations were grouped to represent regions (See Table 5.3: Southern Atlantic-AT, Montréal-MO, rural Québec-QE, Toronto-TO, southwestern rural Ontario-SW, Prairies-PR and Vancouver/LFV-VA, Michigan-MI and northern Ohio-OH) or unique site types (elevated: Toronto's CN Tower-CN and Whiteface Mountain-WF; Ontario lakeshore-LS; rural-remote: Hawkeye Lake-HA and Experimental Lakes Area, (ELA)-EL). Urban sites used for the group analyses were selected primarily on the basis of data completeness, although sites with mean NO concentrations greater than 25 ppb were excluded. Because of the strong gradient in ozone concentrations in Vancouver, only sites in the eastern portion of the city and in the Lower Fraser Valley were included in the Vancouver group. The regional analysis is not presented here; readers are referred to the Report of the Data Analysis Working Group (Multistakeholder NO_x/VOC Science Program, 1997).

For the Canadian sites, mean ozone concentrations ranged from 6.1 ppb (Vancouver-Robson and Hornby) to 44.3 ppb (Long Point). As shown in many studies, mean and median ozone concentrations are highest at rural sites and lowest at downtown urban sites (McKendry, 1993). A look at the lower end of the distribution also shows this difference between rural and urban sites. 25th percentile values of 0-5 ppb are not uncommon at urban sites in B.C. (Vancouver) and Southern Ontario (Toronto, Ottawa), whereas the highest 25th percentile ozone concentration of 28 ppb was recorded at the rural Long Point site. The highest maximum hourly ozone concentrations in the database is 213 ppb, recorded at the Vancouver, Hamilton and Paisley site in 1988. A number of sites in Toronto and southwestern Ontario have experienced maximum ozone concentrations of 170 ppb or greater. The elevated site at Toronto's CN Tower (440 m above the ground) recorded a median ozone concentration of 37 ppb and a 25th percentile value of 24 ppb.

Table 5.3 Ozone Concentration Percentiles (ppb) for May-Sept. 1986 to 1993 - Selected Canadian Sites

Station	City/Province	Address	Reg'n	Start	Stop	% Data	5th	10th	25th	50th	75th	90th	95th	98th	99th	99.9th	Max.	Mean	Std Dev.
10102	St. John's, Nfld.	354 Water Street		5/1/1989	9/30/1993	49	3	6	12	18	25	32	38	49	59	86	97	19.3	11.4
10201	Cormack, Nfld.	Cormack		5/1/1989	9/30/1993	47	10	12	17	23	29	36	40	46	50	61	70	23.6	9.4
20201	North Cape, PEI	North Cape		9/17/1992	9/30/1993	14	16	18	22	27	33	41	49	55	59	88	89	28.6	10.0
30115	Halifax, NS	CFB Shearwater		5/1/1986	9/30/1993	63	6	10	17	25	35	44	50	58	64	80	100	26.3	13.6
30501	Kejimkujik, NS	National Park	AT	5/1/1986	9/30/1992	82	8	11	17	25	34	44	52	64	71	96	150	26.8	13.8
40202	Saint John, NB	Post Office		5/1/1986	9/30/1991	67	2	9	12	20	30	44	51	64	70	100	116	24.7	15.5
40203	Saint John, NB	Forest Hills	AT	5/6/1986	9/30/1993	92	4	9	15	23	32	41	50	60	68	90	113	25.0	14.1
40401	Fundy Nat. Park, NB	Hastings Tower	AT	6/9/1989	9/26/1993	47	16	18	23	30	39	50	58	67	75	92	117	32.4	13.2
40501	Point Lepreau, NB	Main Gate	AT	7/15/1986	9/30/1993	69	0	1	10	24	36	50	60	76	86	122	145	26.0	18.9
40601	Blissville, NB	Airport Road	AT	7/2/1987	9/30/1993	67	0	3	10	20	32	46	56	70	80	114	137	24.3	17.5
40701	Norton, NB	Ball Park	AT	6/5/1989	9/30/1993	50	0	2	12	23	34	45	52	62	69	88	107	24.1	16.0
50102	Montreal, QC	Jardin Botanique	MO	5/1/1986	9/25/1993	82	0	0	10	20	30	40	50	60	70	90	130	18.9	16.5
50103	Montreal, QC	Pointe-Aux -Trembles	MO	5/1/1986	9/30/1993	86	0	0	10	20	30	40	50	60	70	100	130	19.7	17.1
50104	Montreal, QC	1125 Ontario Est	MO	5/1/1986	9/30/1993	91	0	0	10	20	30	40	50	70	70	100	120	19.2	17.1
50110	Montreal, QC	Parc Pilon, Mtl.-Nord	MO	6/1/1986	9/30/1993	84	0	0	10	20	30	50	60	70	80	110	160	20.7	19.2
50113	Montreal, QC	Pie X & Cardinal	MO	5/1/1986	9/30/1993	75	0	0	10	20	30	50	60	70	80	110	130	23.0	19.0
50115	Montreal, QC	1001 Boul Maisonneuve O.		5/1/1986	9/30/1993	89	0	0	0	10	10	20	30	40	50	70	90	9.4	11.5
50116	Montreal, QC	3161 Joseph, Verdun	MO	5/1/1986	9/29/1993	92	0	0	10	20	30	40	60	70	80	100	120	20.7	18.1
50119	Montreal, QC	699 Cure Poirier		6/3/1986	9/30/1993	70	0	0	10	20	30	40	50	60	70	100	130	20.7	17.5
50307	Québec, QC	Parc Cartier Breboeuf		5/1/1986	9/30/1993	87	0	0	0	10	20	30	40	50	50	70	80	13.5	12.4
51501	St. Zephrin, QC		QE	5/21/1987	9/30/1993	46	5	10	16	23	36	50	60	69	71	90	95	26.6	15.8
52001	Charette, QC		QE	5/1/1989	9/30/1993	40	0	10	10	20	30	40	50	60	70	110	140	22.4	15.3
52201	St. Simon, QC		QE	6/2/1989	9/30/1993	40	0	10	10	20	40	50	60	70	70	90	100	25.4	16.6
52301	Faustin, QC		QE	5/1/1990	9/30/1993	35	10	20	20	30	40	50	60	70	80	90	100	31.4	14.7

Table 5.3 Ozone Concentration Percentiles (ppb) for May-Sept. 1986 to 1993 – Selected Canadian Sites

Station	City/Province	Address	Reg'n	Start	Stop	% Data	5th	10th	25th	50th	75th	90th	95th	98th	99th	99.9th	Max.	Mean	Std Dev.
52401	La Peche, QC		QE	5/1/1989	9/30/1993	37	0	10	10	30	40	50	60	70	70	90	100	27.0	16.6
54001	Montmorency, QC		QE	5/31/1988	9/30/1992	49	9	13	19	26	35	44	50	59	66	87	99	27.7	12.7
60101	Ottawa, ON	88 Slater St.		5/1/1986	9/30/1993	85	1	2	5	9	16	24	29	36	41	57	78	11.5	9.2
60104	Ottawa, ON	Rideau & Wurtemburg		5/1/1986	9/30/1993	96	2	4	11	20	31	44	53	64	71	95	127	22.7	15.9
60204	Windsor, ON	467 University Ave. West		5/1/1986	9/30/1993	96	1	3	10	23	38	55	67	80	88	112	159	26.6	20.7
60302	Kingston, ON	Napier Street		6/14/1988	9/29/1993	48	0	2	14	26	39	55	66	80	88	112	140	28.1	20.0
60403	Toronto, ON	Evans & Arnold Ave.		5/1/1986	9/30/1993	95	0	1	5	15	29	46	57	70	78	100	157	19.7	18.5
60410	Toronto, ON	Lawrence & Kennedy	TO	5/1/1986	9/30/1993	97	0	1	8	20	33	48	59	73	83	112	162	23.0	19.1
60413	Toronto, ON	Elmcrest Road	TO	5/1/1986	9/30/1993	97	0	0	5	19	33	50	62	77	86	113	148	22.4	20.4
60415	Toronto, ON	Queensway W & Hurontario	TO	5/1/1986	9/30/1993	96	0	2	8	20	34	49	61	75	84	113	177	23.5	19.2
60417	Toronto, ON	26 Breadalbane St.		5/1/1986	9/30/1990	59	1	2	9	19	32	48	60	74	83	111	159	22.9	18.8
60418	Toronto, ON	Junction Triangle	TO	5/1/1986	9/30/1993	93	1	3	8	21	36	51	64	77	86	112	178	24.6	20.0
60419	Toronto, ON	CN Tower	CN	5/1/1986	9/30/1993	92	6	12	24	37	53	71	82	94	103	138	196	39.9	22.7
60421	Toronto, ON	Yonge St. & Finch St.		6/1/1988	9/30/1993	71	0	2	9	21	34	49	61	76	87	117	177	24.0	19.4
60512	Hamilton, ON	Elgin & Kelly		5/1/1987	9/30/1993	87	0	2	9	21	35	50	61	75	83	108	137	24.1	19.2
60513	Hamilton, ON	Vickers Rd. & East 18th St.		5/1/1986	9/30/1993	98	0	3	12	25	40	56	67	79	85	107	131	28.0	20.4
60514	Hamilton, ON	Nash Rd. & Kentley Dr.		5/1/1986	9/30/1993	96	0	2	11	24	39	54	64	76	86	108	128	26.8	20.1
60607	Sudbury, ON	Science Centre North		5/1/1988	9/30/1993	73	8	12	19	28	38	51	60	71	77	95	113	30.1	15.6
60707	Sault Ste. Marie, ON	Wm. Merrifield School		5/1/1987	9/30/1993	82	2	5	13	23	33	43	50	59	65	84	102	24.0	14.6
60807	Thunder Bay, ON	615 James St. S.		5/12/1987	9/30/1993	85	0	1	7	18	27	36	42	49	54	68	77	18.5	13.2
60901	London, ON	King & Rectory		5/1/1986	9/30/1993	96	2	5	15	27	41	56	66	77	84	108	137	29.5	19.6
61004	Sarnia, ON	Front St. At CN Tracks		5/1/1986	9/30/1993	97	3	7	16	25	38	53	63	77	86	112	170	28.3	18.4
61005	Sarnia, ON	MTC Shed	SW	5/1/1986	9/30/1993	96	8	12	19	29	42	58	71	84	93	114	146	32.6	19.2
61201	Cornwall, ON	Bedford & Third St.		5/1/1986	9/30/1993	97	3	6	14	24	36	48	57	68	75	94	127	26.3	16.7
61302	St. Catherines, ON	Argyle Crescent		5/1/1988	9/30/1993	73	1	4	14	27	42	57	67	76	82	105	132	29.5	20.1

Table 5.3 Ozone Concentration Percentiles (ppb) for May-Sept. 1986 to 1993 – Selected Canadian Sites

Station	City/Province	Address	Reg'n	Start	Stop	% Data	5th	10th	25th	50th	75th	90th	95th	98th	99th	99.9th	Max.	Mean	Std Dev.
61501	Kitchener, ON	Edna & Frederick		5/1/1986	7/5/1990	53	1	4	11	22	37	54	66	78	88	109	118	26.1	19.9
61502	Kitchener, ON	West Ave. & Homewood		7/6/1990	9/30/1993	42	2	6	16	28	41	55	64	74	80	97	118	29.6	18.5
61602	Oakville, ON	Bronte Rd. & Woburn Cr.		5/1/1986	9/30/1993	95	0	2	10	24	39	54	65	79	88	118	183	26.7	20.8
61701	Oshawa, ON	Ritson Rd. & Olive Ave.		5/1/1986	9/30/1993	92	2	4	12	23	34	48	60	75	86	112	185	25.3	18.2
61802	Guelph, ON	Exhibition & Clark St.		5/1/1986	9/30/1993	91	2	6	16	27	42	57	68	80	87	103	117	30.2	19.8
62001	North Bay, ON	OPP. Station		5/1/1989	9/30/1993	61	3	6	16	26	37	50	59	69	76	90	103	27.7	16.8
62101	Huron Park, ON	College Of Agriculture		5/1/1986	9/30/1991	62	9	13	20	31	45	61	71	82	90	112	127	34.1	19.1
62201	Merlin, ON	MOE Water Pump Stn.	SW	5/1/1986	9/30/1993	96	6	10	19	31	45	61	72	85	93	119	133	33.8	20.3
62401	Parkhill, ON	PUC Bldg.	SW	5/1/1986	9/30/1993	97	6	11	19	30	44	60	71	84	94	116	144	33.3	20.0
62501	Tiverton, ON	Con. Rd. 2 Lot A	LS	5/1/1986	9/30/1993	97	10	15	23	33	46	63	76	91	100	126	156	36.6	19.8
62601	Simcoe, ON	Experimental Farm	SW	5/1/1986	9/30/1993	89	10	14	22	33	47	62	71	84	93	119	190	36.0	19.3
62701	Long Point, ON	Provincial Park	LS	5/1/1986	9/30/1993	87	15	20	28	41	57	74	86	101	113	136	189	44.3	22.3
62901	Niagara Falls, ON	Allendale Ave.		5/18/1988	9/30/1993	60	6	10	19	31	46	63	73	85	92	116	139	34.2	20.6
63001	Burlington, ON	Hwy. 2 & N. Shore Blvd.		5/1/1986	9/30/1993	96	2	4	12	24	39	54	65	77	85	114	167	27.4	19.8
63101	Alliston, ON	509 Victoria Street E		5/1/1986	9/30/1993	95	2	4	13	24	36	50	60	70	77	95	177	26.2	17.5
63201	Stouffville, ON	Hwy. 47 & Hwy. 48	TO	5/1/1986	9/30/1993	94	7	11	18	27	39	52	63	76	84	113	161	30.0	17.3
63301	Dorset, ON	Hwy. 117 & Paint Lake Rd		5/1/1986	9/30/1991	66	6	9	18	29	41	55	66	77	83	100	138	31.1	18.0
63401	Hawkeye Lk., ON	Hawkeye Lake	HA	5/1/1986	9/30/1991	56	4	8	16	25	35	48	56	65	70	82	95	26.7	15.4
64001	ELA., ON	Experimental Lakes Area	EL	5/9/1988	9/30/1992	50	14	17	23	30	39	47	53	59	63	74	81	31.6	11.8
64101	Algoma, ON			5/17/1988	9/30/1992	57	12	15	21	29	40	52	62	74	83	100	108	31.7	15.6
64201	Chalk River, ON			5/17/1988	9/30/1992	44	7	11	18	26	37	48	58	70	77	90	96	28.6	15.2
64401	Egbert, ON			7/26/1988	9/30/1992	54	11	14	21	31	43	57	67	76	82	98	138	33.5	16.9
70118	Winnipeg, MB	Jefferson & Scotia		5/1/1986	9/30/1993	91	2	5	12	22	33	44	50	59	64	77	98	23.5	15.0
70119	Winnipeg, MB	65 Ellen Street	PR	5/1/1986	9/30/1993	84	1	3	9	18	29	39	46	53	59	74	100	20.2	14.0
70203	Brandon, MB	1430 Victoria Ave. E.		5/1/1987	9/10/1993	77	6	9	16	24	34	44	50	57	61	70	78	25.7	13.4
80110	Regina, SK	2505 11th Avenue	PR	5/1/1987	9/30/1993	85	3	6	11	19	28	36	41	46	50	62	99	20.3	11.6

Table 5.3 Ozone Concentration Percentiles (ppb) for May-Sept. 1986 to 1993 - Selected Canadian Sites

Station	City/Province	Address	Reg'n	Start	Stop	% Data	5th	10th	25th	50th	75th	90th	95th	98th	99th	99.9th	Max.	Mean	Std Dev.
80209	Saskatoon, SK	Idylwyld Dr. & 33rd St.	PR	5/1/1986	9/30/1992	80	4	6	13	20	29	38	43	47	50	59	68	21.4	11.8
90122	Edmonton, AB	127 St. & 133 Avenue	PR	5/1/1986	9/30/1993	99	1	2	10	21	34	45	51	58	62	75	102	22.9	15.9
90130	Edmonton, AB	10255 - 104th Street		5/1/1986	9/30/1993	100	3	5	11	20	30	39	44	49	53	64	93	21.3	12.7
90222	Calgary, AB	39 St. & 29 Ave. NW	PR	5/1/1986	9/30/1993	99	3	6	15	27	38	48	52	58	62	77	106	26.9	15.4
90227	Calgary, AB	611-4th Street SW		5/1/1986	9/30/1993	99	2	3	8	17	27	36	41	46	50	61	79	18.3	12.4
90701	Fort MacMurray, AB	Macdonald Drive		7/1/1986	9/30/1993	80	2	5	11	21	33	45	51	60	65	77	128	23.2	15.3
100108	Vancouver, BC	250 West 70th Avenue		5/1/1986	5/6/1993	69	0	1	3	12	23	31	36	42	47	62	81	14.0	12.2
100110	Vancouver, BC	E. Hastings & Kensington	VA	5/1/1986	9/30/1993	95	0	1	5	12	22	31	36	43	49	76	105	14.6	11.9
100111	Vancouver, BC	Rocky Pt. Park	VA	5/1/1986	9/30/1993	96	0	0	1	11	26	38	46	57	64	98	149	15.6	16.2
100112	Vancouver, BC	Robson/Hornby		5/1/1986	9/30/1993	93	0	0	1	3	10	16	20	25	28	42	57	6.1	6.8
100118	Vancouver, BC	2550 West 10th Avenue		5/1/1987	9/30/1993	81	0	0	1	11	24	34	39	46	52	71	88	14.2	13.7
100120	Vancouver, BC	Willingdon & Penzanc, Burnaby	VA	5/1/1986	9/30/1993	94	0	1	5	14	25	34	40	48	55	83	105	16.4	13.2
100121	Vancouver, BC	75 Riverside Dr. NVan.		5/1/1986	9/30/1993	90	0	1	4	10	17	25	30	36	41	63	93	11.7	9.9
100122	Vancouver, BC	Sunnyside Road, Anmore	VA	5/1/1986	9/30/1993	97	2	3	8	16	27	38	46	56	65	101	156	19.0	14.6
100123	Vancouver, BC	West End Welsh Road, West Van.	VA	5/1/1986	9/30/1993	77	0	0	2	8	20	30	36	42	46	71	95	12.2	12.2
100124	Vancouver, BC	475 Guildford Way, Port Moody	VA	5/1/1986	9/30/1993	98	0	1	3	12	23	35	42	53	61	96	167	15.3	14.5
100125	Vancouver, BC	8544 116th Ave., Delta	VA	5/16/1986	9/30/1993	89	0	1	5	14	23	31	35	41	46	66	96	15.0	11.5
100126	Vancouver, BC	Ring Road, Burnaby	VA	5/7/1986	9/30/1993	96	4	7	13	20	28	37	43	52	59	87	194	21.6	12.4
100127	Vancouver, BC	19000 & 72nd Ave., Surrey	VA	5/1/1986	9/30/1993	93	2	4	10	18	29	39	46	55	61	86	159	20.5	14.1
100128	Vancouver, BC	Williams & Aragon, Richmond		7/1/1986	9/30/1993	89	0	1	4	15	26	34	40	46	51	68	93	16.5	13.3
100129	Vancouver, BC	Hamilton & Paisley		6/8/1987	9/30/1993	80	0	0	3	12	25	36	44	55	64	96	213	15.8	15.3
100130	Vancouver, BC	Sperling & Sprott Ave		5/2/1986	9/30/1992	71	0	0	1	5	19	30	36	43	48	65	94	10.9	12.5
100131	Vancouver, BC	Seymour Falls, North Vancouver		5/5/1986	9/30/1993	82	2	4	9	17	27	38	45	55	63	88	119	19.5	13.8

Table 5.3 Ozone Concentration Percentiles (ppb) for May-Sept. 1986 to 1993 - Selected Canadian Sites

Station	City/Province	Address	Reg'n	Start	Stop	% Data	5th	10th	25th	50th	75th	90th	95th	98th	99th	99.9th	Max.	Mean	Std Dev.
100303	Victoria, BC	1250 Quadra St.		5/1/1986	9/30/1993	51	0	0	8	16	24	32	37	43	46	60	78	16.7	11.5
100701	Kelowna, BC	1000 Klo Rd.		7/1/1987	9/30/1993	53	0	0	10	20	32	40	47	53	56	70	93	21.4	14.8
101001	Abbotsford, BC	Airport		5/1/1986	9/30/1991	68	0	1	6	19	32	43	51	62	72	97	118	21.1	17.1
101101	Chilliwack, BC	Works Yard	VA	5/1/1986	9/30/1993	84	0	0	3	14	28	41	49	60	68	87	104	17.9	16.5
101201	Pitt Meadows, BC	Airport	VA	5/1/1986	9/30/1993	90	0	0	3	15	27	38	45	54	60	83	154	17.2	15.3
102001	Saturna, BC			5/28/1991	9/30/1992	22	13	16	21	26	34	41	46	52	56	65	74	27.8	10.0

5.3.1 Monthly Variation in Daily Mean and Maximum Ozone Concentrations

Averages of daily mean and daily maximum one hour ozone concentrations were calculated for each month to examine seasonal variations in the data. These monthly averages revealed pronounced seasonal variations of ozone at individual stations and regions throughout Canada (Figures 5.3 to 5.6). Considerable variations were observed in the time of year when maximum ozone levels are attained. Sites in Vancouver (Figure 5.3) recorded the lowest mean and maximum ozone levels in the country during the months of October through February. Daily mean ozone peaked in April and May at the sites and declined slowly in the following months. Daily maximum ozone also peaked in April and May but there was little change from May through September at the western Vancouver sites, when the mean daily maximum ozone was in the range of 45 to 50 ppb.

The Calgary and Edmonton sites experienced more pronounced seasonal variation in average daily maximum ozone, with a peak in the month of May. Although average daily maximum and average daily mean ozone concentrations reached their lowest levels at these urban sites during November to January, average concentrations were higher than those recorded in the Vancouver urban area. For these two sites, monthly averages for daily means exceeded 25 ppb in May and the corresponding averages for daily ozone maxima exceeded 50 ppb.

Springtime maxima in ozone concentrations are often observed at remote rural sites in Canada (see Section 5.1; Robichaud & Jacques, 1991; Robichaud, 1993; Leduc & Gagnon, 1992; Fuentes & Dann, 1995; Bottenheim et al., 1994). The observation of springtime ozone maxima at urban sites is contrary to the notion that urban peaks in ozone are a function primarily of elevated photochemical ozone, since production of the latter peaks in the summer. Higher ozone concentrations measured during the spring may reflect the impact of ozone transport from the stratosphere. In western Canada, the tropopause is closest to the ground surface during the spring. As a result, intrusion of ozone-rich air from the lower stratosphere to the upper troposphere can occur. Some researchers (Liu et al., 1987; Logan, 1987) have proposed that because of the longer lifetime of ozone in the winter, the accumulation of anthropogenic precursors may contribute to the spring ozone maximum. The decline in ozone concentrations during the summer months at these locales can be attributed to enhanced sink processes engendered by ozone photolysis and uptake by vegetation. As shown in Figure 5.4, other prairie sites and two sites in northern Ontario also experienced April to May peaks in mean and mean daily maximum ozone. Unlike the prairie urban sites, the Hawkeye Lake site registered an increase in average daily maximum ozone in July. The Experimental Lakes Area site showed the smallest divergence between the daily mean and daily maximum plots.

Figure 5.3 Monthly Averages of Daily Mean and Daily Maximum One Hour Ozone (ppb) (1986 to 1993) – British Columbia and Alberta

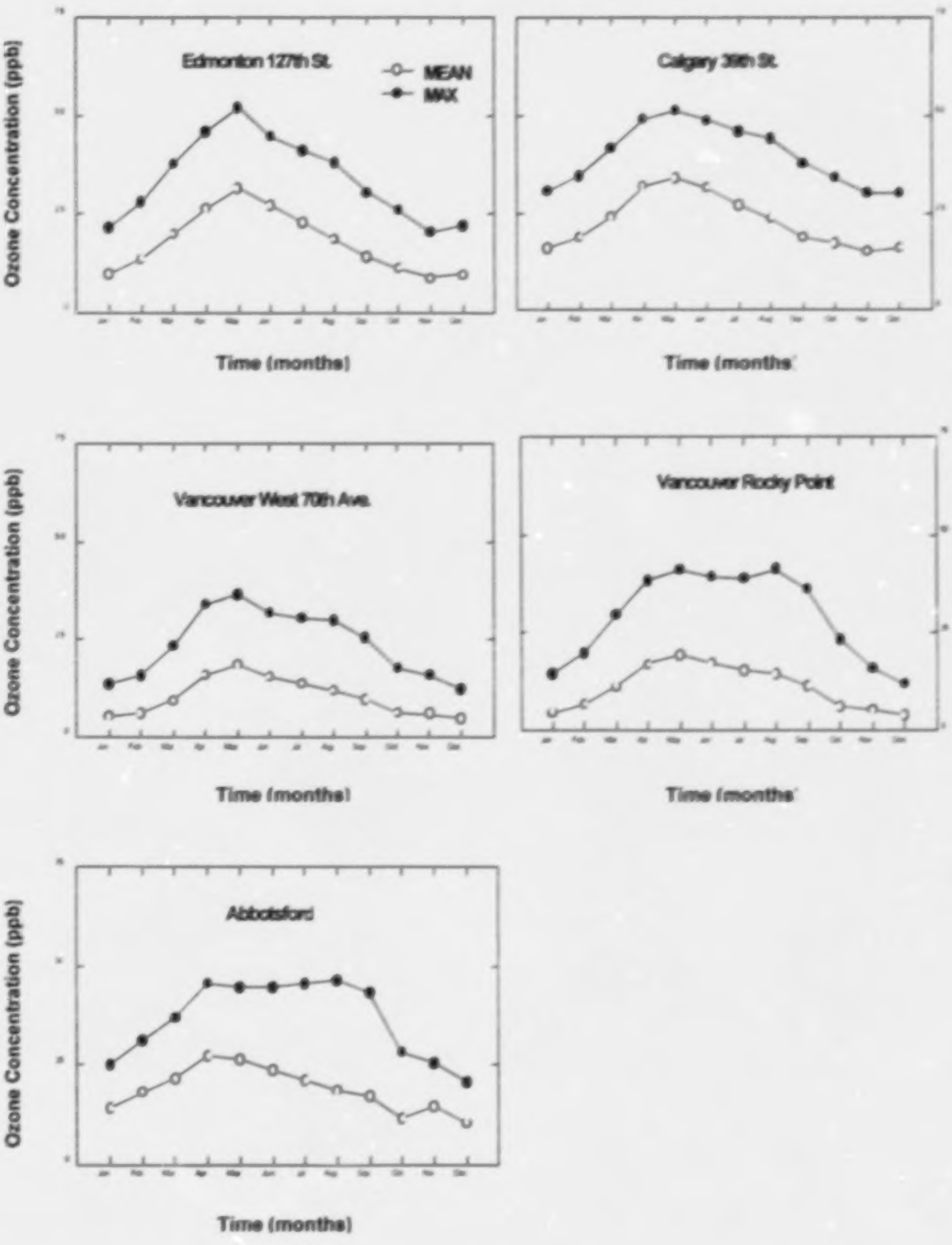
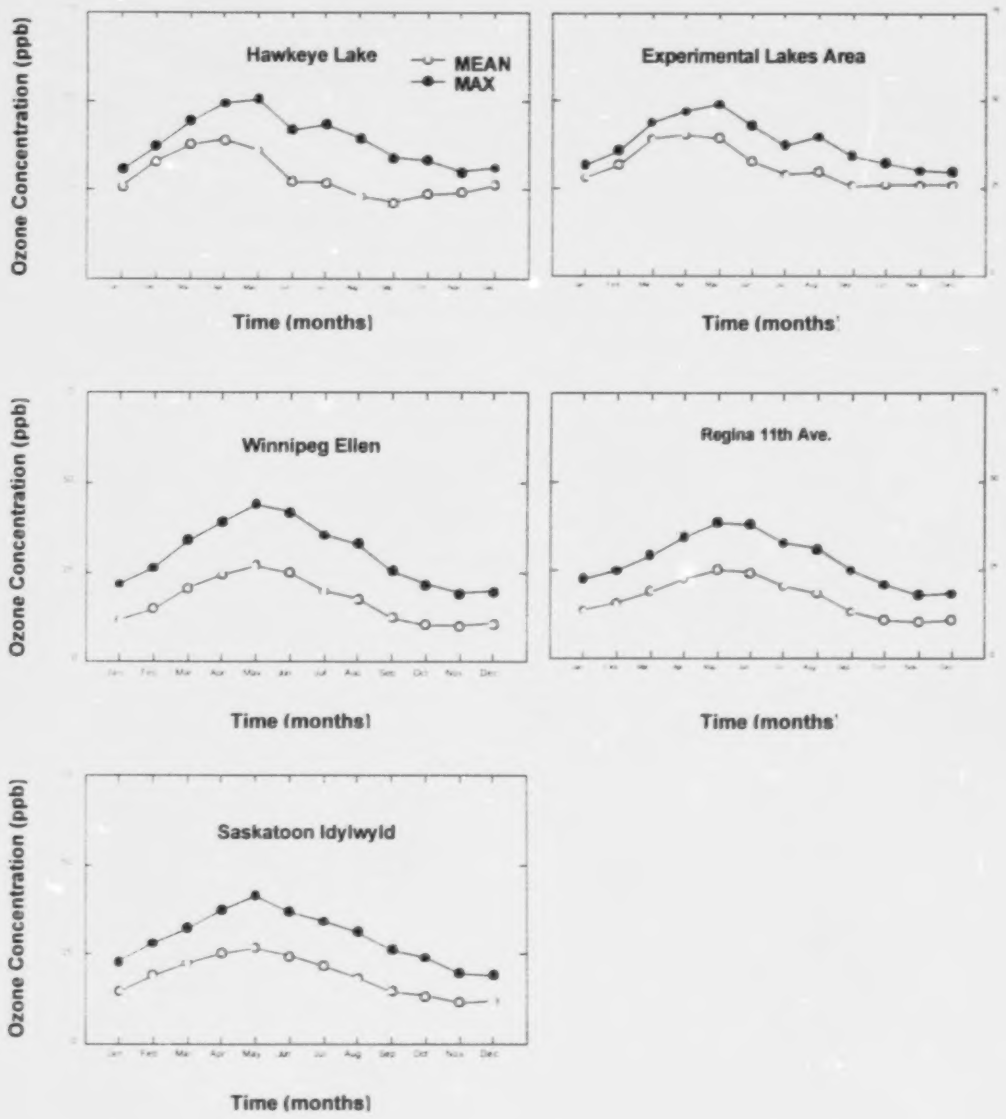


Figure 5.4 Monthly Averages of Daily Mean and Daily Maximum One Hour Ozone (ppb) (1986 to 1993) – Saskatchewan, Manitoba and Northern Ontario



Urban and rural stations in environments under considerable anthropogenic influence showed the highest monthly concentrations from June to August (see Figure 5.5). In southwestern rural Ontario, the long-range transport of pollutants can contribute significantly to enhanced ozone levels measured during June to August. Summer-time maximum ozone concentrations were significantly higher than those recorded at the western sites. All the sites shown in Figure 5.5 recorded maximum monthly ozone concentrations in July, with mean daily maxima ranging from 55 to 65 ppb. The elevated CN Tower site showed a larger amplitude than any of the surface sites in the seasonal pattern of both mean and daily maximum ozone.

The Montréal urban sites (Figure 5.6) also experienced the highest monthly ozone in July, although mean and daily maximum ozone concentrations were lower than at the Toronto sites. The rural site of St. Zephrin (located between Montréal and Québec City; 1989 to 1993 data only) showed a much different seasonal pattern, with maximum monthly ozone recorded in March and little variation in the daily maximum between March and August. Mean and mean daily maximum ozone concentrations were substantially higher at this site, as compared to the Montréal sites, for the months of March through June.

Little seasonal variation in the monthly averaged ozone concentrations occurred in the Southern Atlantic region, as represented by the data for Saint John and Kejimkujik (Figure 5.6). In contrast to the Toronto and Montréal sites, ozone levels at the Saint John site remained high during winter. The overall seasonal pattern of ozone in Saint John is similar to that of the Kejimkujik site, indicating that the Southern Atlantic region of Canada is influenced by air masses whose ozone concentrations differ markedly from those affecting Ontario and Québec.

Figure 5.5 Monthly Averages of Daily Mean and Daily Maximum One Hour Ozone (ppb) (1986 to 1993) - Toronto and Southern Ontario

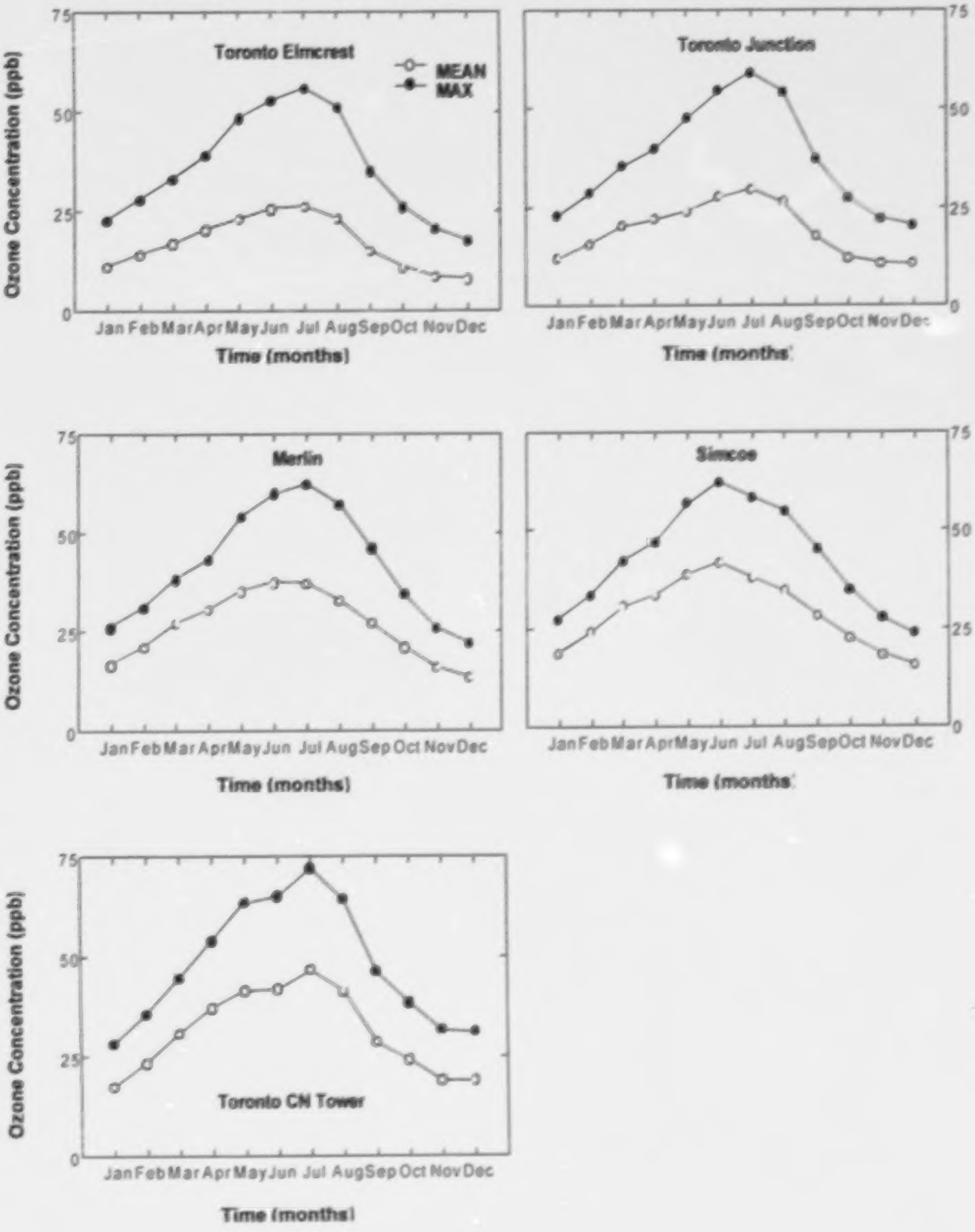
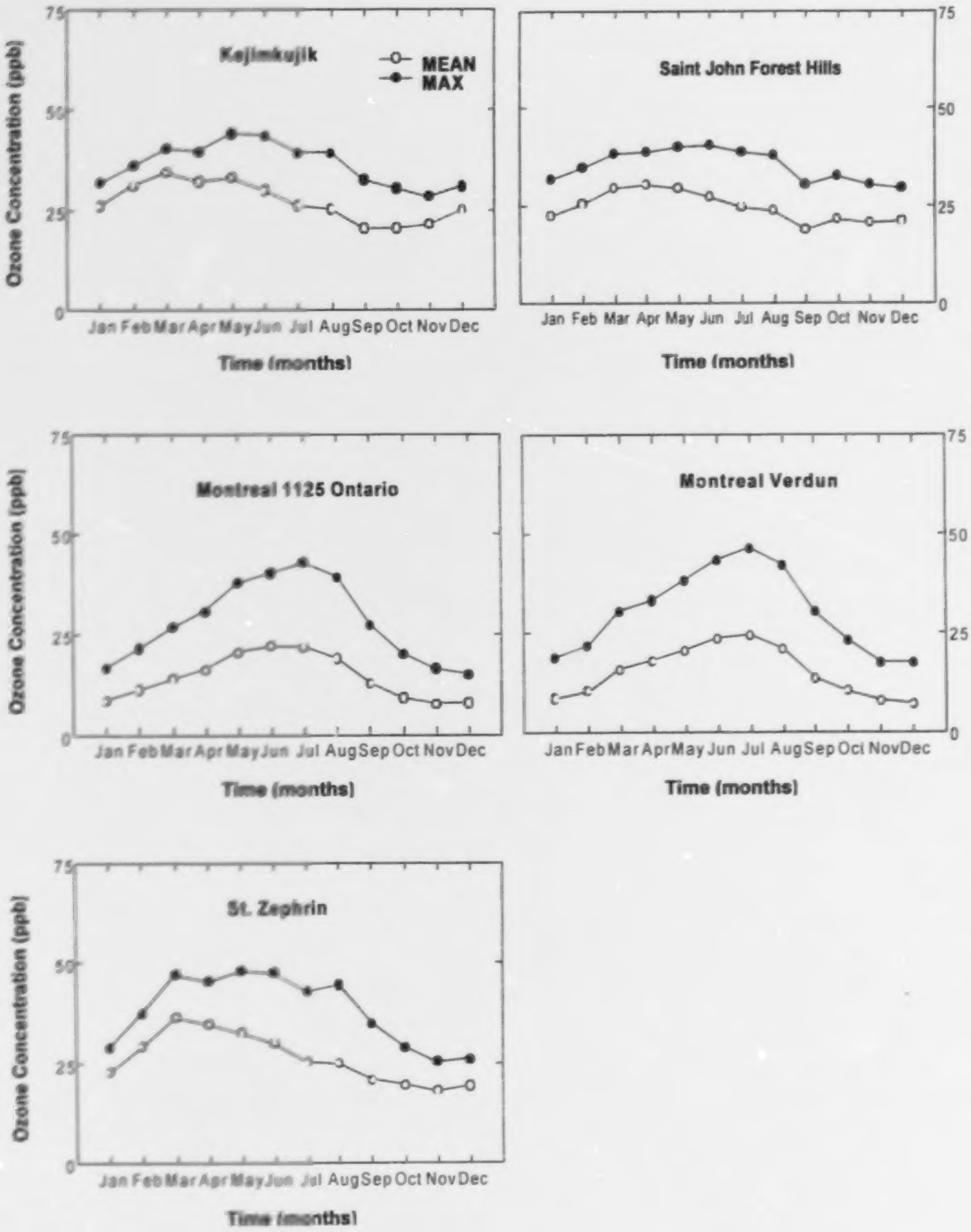


Figure 5.6 Monthly Averages of Daily Mean and Daily Maximum One Hour Ozone (ppb) (1986 to 1993) - Montréal and Southern Atlantic



5.3.2 Diurnal Variation in Ozone Concentrations - Summer and Winter

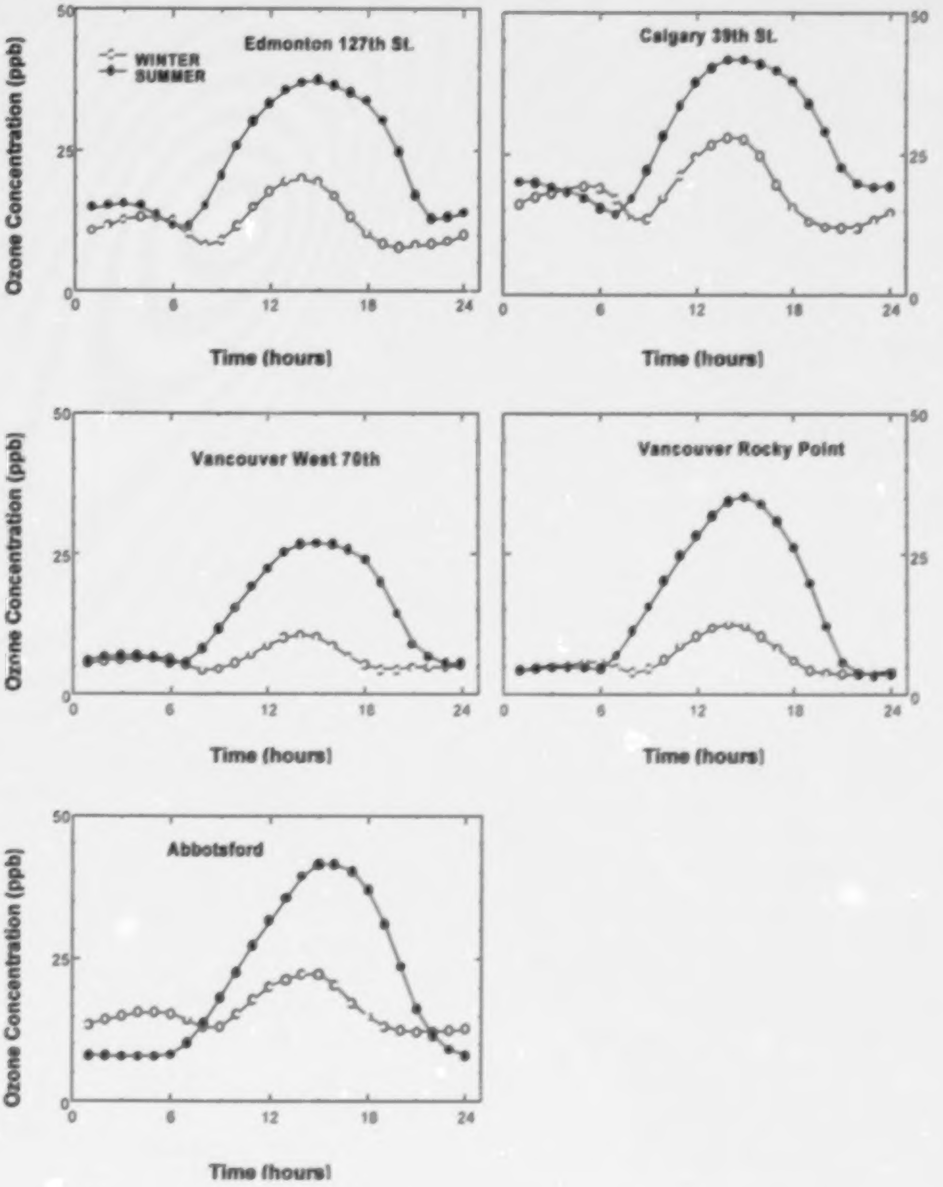
Hourly ozone data for winter and summer time were aggregated separately to compute seasonal averages. "Winter" months were defined to comprise November to March, while "summer" months were defined to include May to September. As expected, large differences exist in the amplitude of diurnal ozone concentration cycles for winter- and summer-time (see Figures 5.7 to 5.10). Ozone levels during winter remain low due to limited photochemistry and exhibit smaller diurnal variations. Most urban sites record mean winter ozone concentrations in the range of 15 to 20 ppb. The rural remote sites of Hawkeye Lake and ELA and the two Southern Atlantic sites had mean winter ozone concentrations of 25 to 30 ppb. The Saint John and Kejimkujik sites showed the smallest variation between summer and winter diurnal profiles, while sites in southern Ontario, Toronto and Vancouver showed the greatest divergence between the summer and winter profiles.

Most urban sites recorded comparable summer and winter nighttime ozone levels. The rural Ontario sites (Parkhill, Merlin, Hawkeye Lake and ELA) recorded higher summer ozone for most hours of the day, with summer-time ozone values approaching winter-time values between 06:00 and 07:00. The elevated CN Tower site showed the largest mean divergence between summer and winter diurnal ozone profiles with an average hourly difference of more than 25 ppb. These variations in diurnal ozone result as a consequence of longer summer days with warm temperatures and the availability of sufficient levels of solar radiation necessary for the ozone photochemistry.

At urban sites, ozone concentrations were much lower during nighttime than daytime. Overall daily mean ozone concentrations in rural locations were greater than those recorded in nearby urban sites and diurnal profiles were much smoother, with higher nighttime ozone concentrations. The shape and amplitude of diurnal ozone concentration cycles are strongly influenced by atmospheric conditions, site location and prevailing NO_x levels. Even in well-defined and "self-contained" airsheds, such as the one in British Columbia's Lower Fraser Valley, diurnal ozone patterns varied appreciably within small spatial scales (Figure 5.7). In this instance, the diurnal ozone differences among these three stations resulted because of site positioning with respect to ozone precursor sources. The Vancouver West 70th site measured lower diurnal ozone levels, with peak summertime values around 25 ppb, compared to the site downwind of Vancouver (Abbotsford) which recorded summertime diurnal maximum values of approximately 40 ppb. Peak ozone levels occurred one hour later at Abbotsford than at Rocky Point (16:00 vs. 15:00) and persisted through 17:00. Advection of ozone and its precursors from the city is undoubtedly contributing to enhanced ozone levels at Abbotsford.

Of the sites in Alberta and British Columbia, (Figure 5.7) the Calgary site showed the largest diurnal variation in summer-time ozone with maximum average concentrations of over 40 ppb. This value is comparable to the Abbotsford afternoon maximum. The long-range transport of pollutants to these sites in western Canada has a negligible effect on locally measured ozone. It is likely that most ozone measured in these jurisdictions comes from background tropospheric and stratospheric sources, and locally produced ozone.

Figure 5.7 Hourly Average Ozone Concentrations (ppb) for Summer and Winter (1986 to 1993) – British Columbia and Alberta



The most dynamic ozone patterns in Canada, with respect to their spatial distributions and temporal variations, are experienced in southwestern Ontario. Substantial spatial and temporal ozone changes occur because of the combined influence of precursors existing within the region and the long-distance transport of ozone and its precursors. Southwestern Ontario is geographically situated downwind of major ozone precursor source areas in the Great Lakes region. Additionally, meteorological conditions conducive to elevated ozone levels generally result in southwesterly flows. A rural upwind site (Simcoe), one urban site within the city of Toronto (Junction) and two urban downwind sites (Stouffville and Oshawa) are shown in Figure 5.11 to illustrate the spatial and diurnal variations of ground-level ozone observed in southwestern Ontario.

Figure 5.8 Hourly Average Ozone Concentrations (ppb) for Summer and Winter (1986 to 1993) – Saskatchewan, Manitoba and Northern Ontario

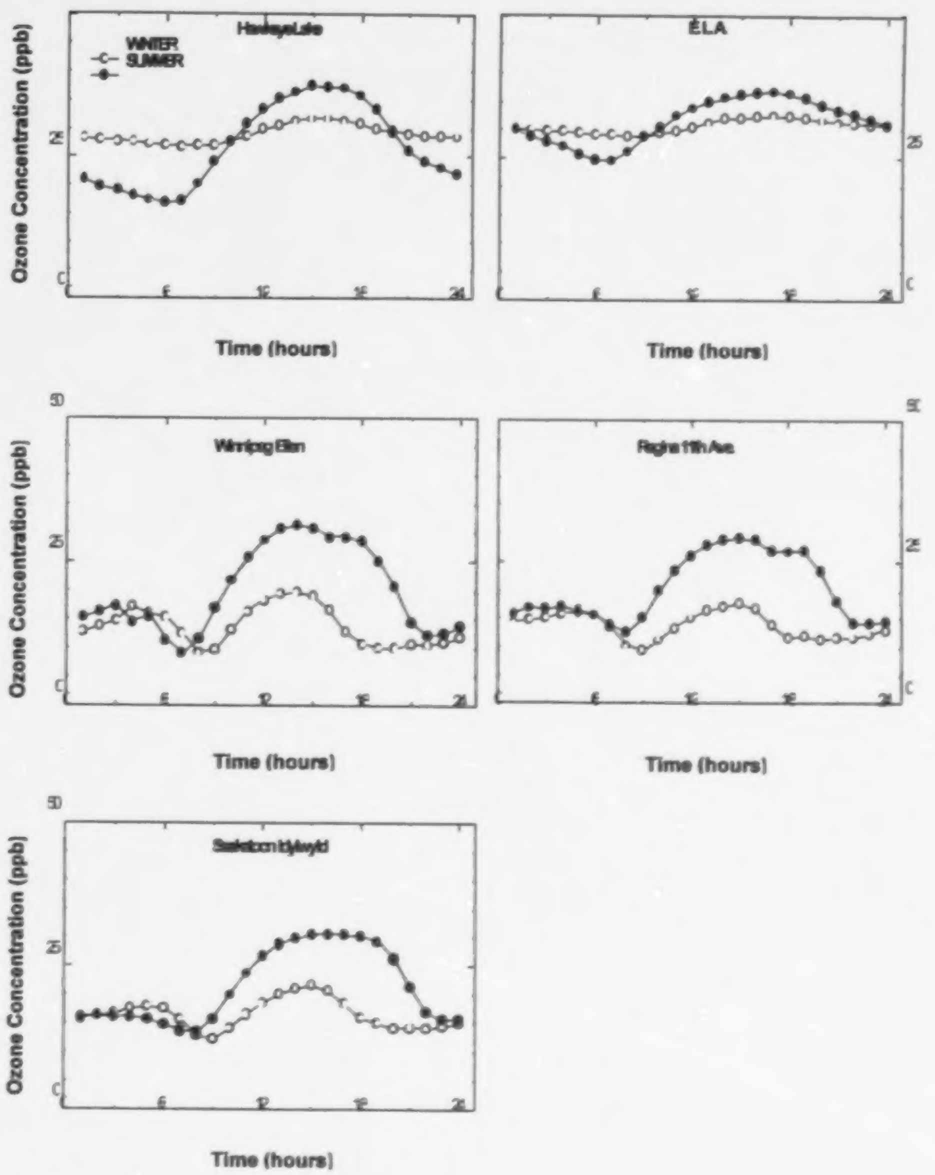
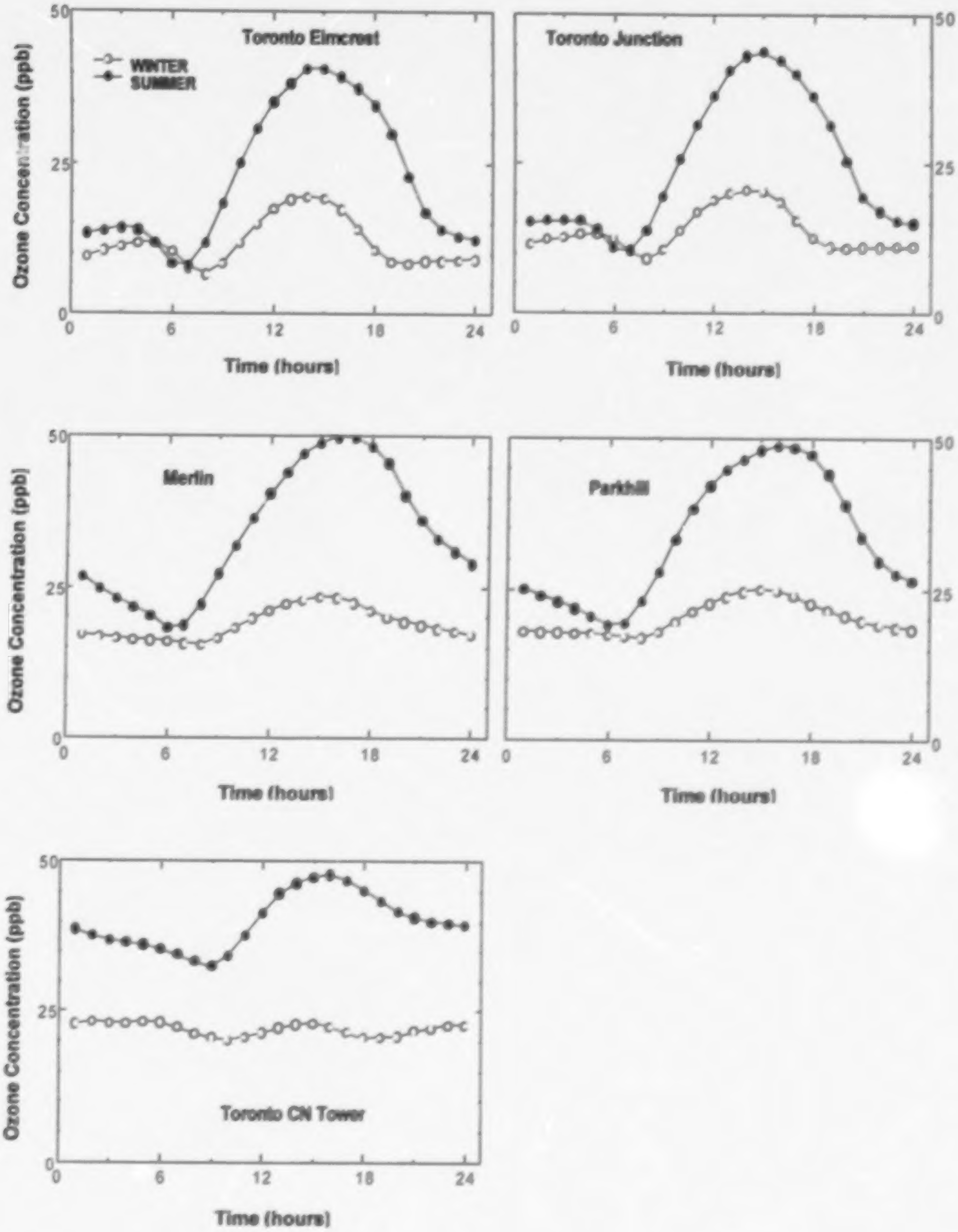


Figure 5.9 Hourly Average Ozone Concentrations (ppb) for Summer and Winter (1986 to 1993) - Toronto and Southern Ontario



At the Simcoe site, ozone levels remained at about 25 ppb and maximum values reached almost 50 ppb during the day. In contrast, the Junction site showed substantially lower nighttime ozone concentrations with minimum values reaching 10 ppb. The Stouffville and Oshawa sites recorded nighttime ozone concentrations higher than Junction but lower than Simcoe. Of these sites, Junction and Stouffville experienced similar maxima (40 ppb). Peaks occurred at the same hour of the day (15:00), but higher concentrations persisted at Stouffville after 17:00. The Oshawa site, although downwind of the Toronto area, recorded average daily maximum ozone values that were approximately 5 ppb lower than Junction.

Summer-time ozone diurnal patterns for Montréal were similar to those for other sites (Figure 5.10); however, diurnal ozone averages were lower in Montréal than in Toronto. McKendry (1993) showed that ozone values in Montréal are lower than in surrounding areas and the city acts as a net ozone sink. Minimum nighttime concentrations approach 10 ppb and maximum daytime levels of approximately 35 ppb sites occur at 14:00. The St. Zephrin site records daily maximum ozone of 40 ppb with a peak at 15:00. It is not clear why Montréal sites experience lower diurnal ozone levels compared to stations elsewhere in the Windsor–Québec City corridor. An examination of nitrogen oxide data for the Montréal area reveals concentrations of the same order of magnitude as for other large cities. One possible reason for apparently lower ozone values in Montréal is that the data are reported to a precision of only 10 ppb.

Diurnal ozone patterns in New Brunswick and Nova Scotia displayed less variation as compared to sites in other parts of Canada (Figure 5.10). This observation applies to both urban and rural environments. For example, ozone data recorded in Saint John displayed little diurnal variation, the difference between maximum and minimum ozone levels amounting to less than 10 ppb. Minimum ozone concentrations stay at around 20 ppb, and maximum levels reach 30 ppb. The diurnal ozone patterns experienced in Saint John resemble those observed in rural environments where substantial ozone is also measured at night. Diurnal ozone levels at the Kejimkujik site showed larger variation with time of day. Nighttime ozone levels are comparable to Saint John and daily maximum values reach 35 ppb. Although smooth diurnal ozone patterns emerge in these data when averaged over long periods, the New Brunswick and Nova Scotia sites are occasionally affected by the long-distance transport of pollutants. This effect of pollutant transport is manifested by intrusions of air masses with ozone concentrations exceeding 100 ppb. These high ozone levels are often measured at night, when there is no local photochemistry.

Figure 5.10 Hourly Average Ozone Concentrations (ppb) for Summer and Winter (1986 to 1993) -Montréal and Southern Atlantic

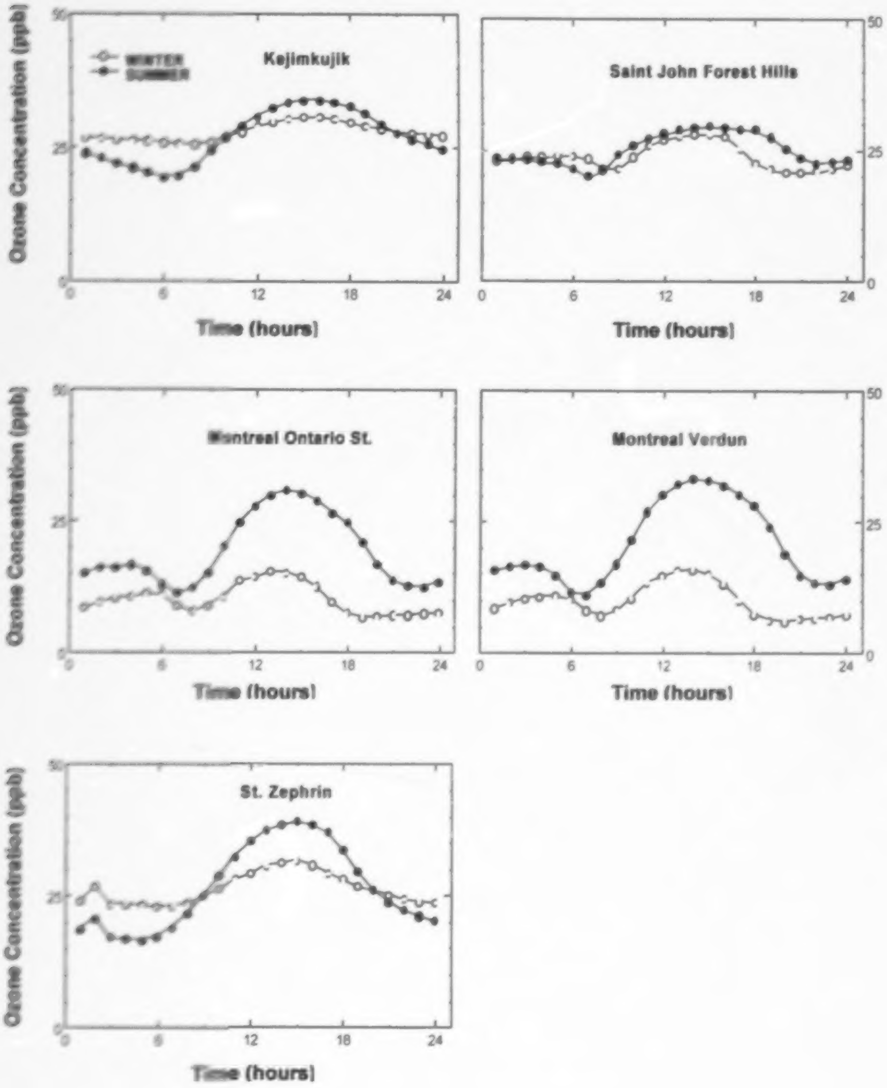
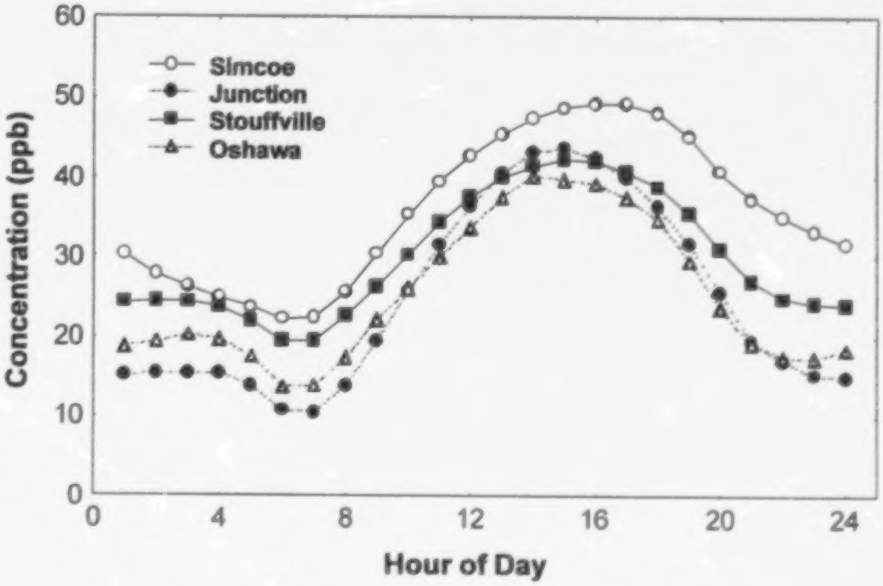


Figure 5.11 Hourly Average Ozone Concentrations (ppb) for Summer (1986 to 1993) - Toronto-Area Sites



5.3.3 The Weekly Cycle of Ozone Daily Maximum and Mean Concentrations

It is known that the ozone precursor emissions have strong temporal variations on several time scales, although many of these are not thoroughly documented. For example, the main source of NO— vehicle traffic—shows a very strong diurnal cycle with a maximum generally in the daylight hours. Superimposed on this is a further modulation, especially in urban areas, related to the maximum traffic flow in the morning and evening rush hours. In addition, this diurnal variation of emissions is different on weekends to that occurring on weekdays. Fewer people go to work on Saturdays, making the morning rush hour weaker, but shopping trips increase automobile traffic during the day. On Sunday, the pattern is very different again, with little early morning traffic and a steadier flow during the rest of the day. These changes in the precursor emission patterns suggest that especially during the daylight hours, ozone concentrations might show significant differences in weekend versus weekday behaviour. Several approaches were taken by the Data Analysis Working Group (Multistakeholder NO_x/VOC Science Program, 1997) to investigate this possibility. Only the results of some of the analyses are reproduced here.

First, at all stations with long records, the average of the daily maximum for each day of the week was determined. This analysis showed that, indeed, at many sites, the average maximum ozone was higher on Saturday and Sunday than on weekdays, particularly those in the large urban centres. More specifically:

- At many sites in the major urban centres (Montréal, Toronto and Vancouver), the mean maximum ozone on the weekend is 10 to 20%—and sometimes 20 to 35%—higher than on weekdays.
- At other large urban centres, the mean maximum ozone is elevated by up to 20% on weekends.
- Winnipeg and Saskatoon are exceptions, with very little difference on weekends.
- At non-urban sites in southern Ontario but in regions potentially affected by the transport of ozone and its precursors from nearby urban centres, there is a consistent weekend increase in the daily maxima of about 4 to 8%—except for Cornwall, with essentially no change.
- In the Atlantic provinces, the weekend change is small, at between -2 and +3%.

Ozone data for selected sites were then aggregated to represent diurnal variations during weekdays (Tuesday through Thursday) and weekends (Saturdays and Sundays) for the summer months and the results are shown in Figures 5.12 to 5.15. Previous studies (Fuentes & Dann, 1993; Pryor et al., 1995; Altshuler et al., 1995) have shown substantial differences between weekdays and weekends in urban diurnal ozone profiles. Reduced NO concentrations on weekends are the primary reason for the different profiles, and the effect should therefore be most pronounced at monitoring sites in major urban centres; particularly those located close to busy, main traffic arteries. As shown in the Figures, a number of major urban sites with high NO concentrations (e.g. Montréal - Ontario, Montréal - Verdun and Vancouver - West 70th) experience the largest increase in afternoon maximum ozone when weekends are compared to weekdays. These sites also show a large increase in ozone between the hours of 05:00-10:00

on weekends. Most sites show higher ozone concentrations during daylight hours on weekends versus weekdays. ELA and Abbotsford show slightly higher (statistical significance not tested) afternoon ozone concentrations on weekdays and Hawkeye Lake, Kejimkujik and Saint John show little difference between weekday and weekend profiles.

It should be noted that this examination of ozone behaviour on weekends versus weekdays is based on the concurrent NO and NO_2 data and does not include consideration of the daily and weekly cycle of VOC concentrations. Such measurements are not available on the same time scales as for ozone and NO_x. Where information on VOC concentrations has been available, some investigators have been able to show that changes in VOC concentrations also influence the diurnal and weekly cycles of ozone (Altshuler et al., 1995).

5.3.4 Summary

Analyses of the monthly variation in ozone concentration (monthly averages of daily mean and daily maximum 1 hr. values) revealed pronounced seasonal variations in ozone concentrations at individual sites and regions across Canada, as well as variations in the time of year when maximum ozone levels are observed. Concentrations clearly peak much earlier in Western Canada (May) than they do in Central Canada (July). In southwestern rural Ontario, summertime maximum ozone levels are significantly higher than those recorded at other Canadian sites. Much less seasonal variation in ozone concentrations occurs in the Atlantic Region. Higher ozone concentrations measured during the spring may reflect the impact of ozone transport from the stratosphere. In Western Canada, the tropopause (boundary between the stratosphere and the troposphere) is closest to the ground during the spring. As a result, occasional intrusion of ozone-rich air from the lower stratosphere can occur.

Analyses of the diurnal cycle show that at urban sites, ozone concentrations are much lower during nighttime than daytime. Overall daily mean ozone concentrations in rural locations are greater than those recorded in nearby urban sites and diurnal cycles are much smoother, with higher nighttime ozone concentrations. The shape and amplitude of hourly ozone concentrations is strongly influenced by atmospheric conditions, site location and prevailing NO_x levels. Sites with high NO levels experience significantly higher mean afternoon maximum ozone on weekends (when NO concentrations are lower) than on weekdays. At these sites, the increase in ozone is observed during all daylight hours on weekends. This is attributed to the lower NO emissions and hence less titration of ozone. This "weekend effect" is also present, but not as strong, at rural sites close to urban areas, and diminishes rapidly with distance downwind. There are substantial year-to-year variations in ozone maxima at the different sites. Much of this variability is a result of yearly change in meteorological factors.

Figure 5.12 Hourly Average Ozone Concentrations (ppb) for Weekdays and Weekends (May to September, 1986-1993)- Alberta and British Columbia

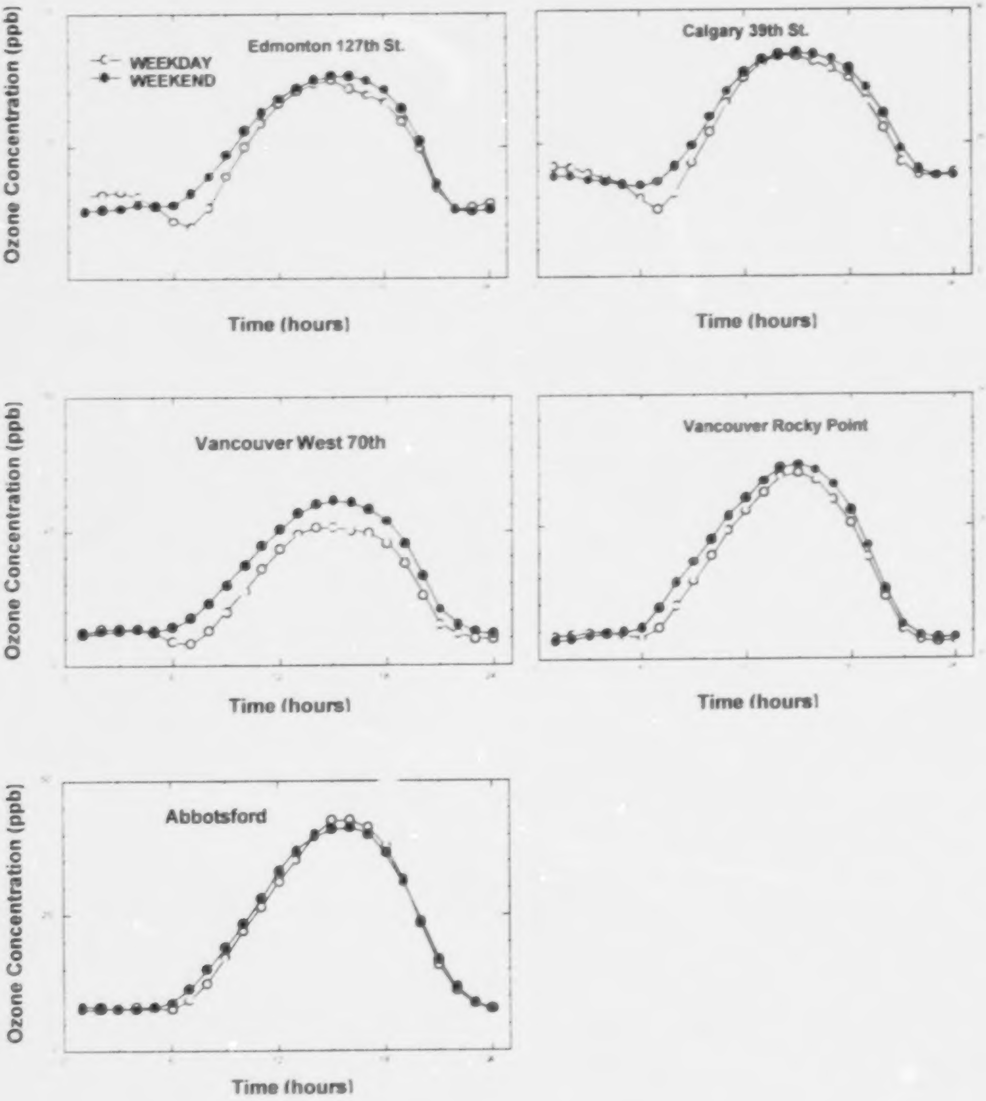


Figure 5.13 Hourly Average Ozone Concentrations (ppb) for Weekdays and Weekends (May to September, 1986 to 1993) – Saskatchewan, Manitoba and Northern Ontario

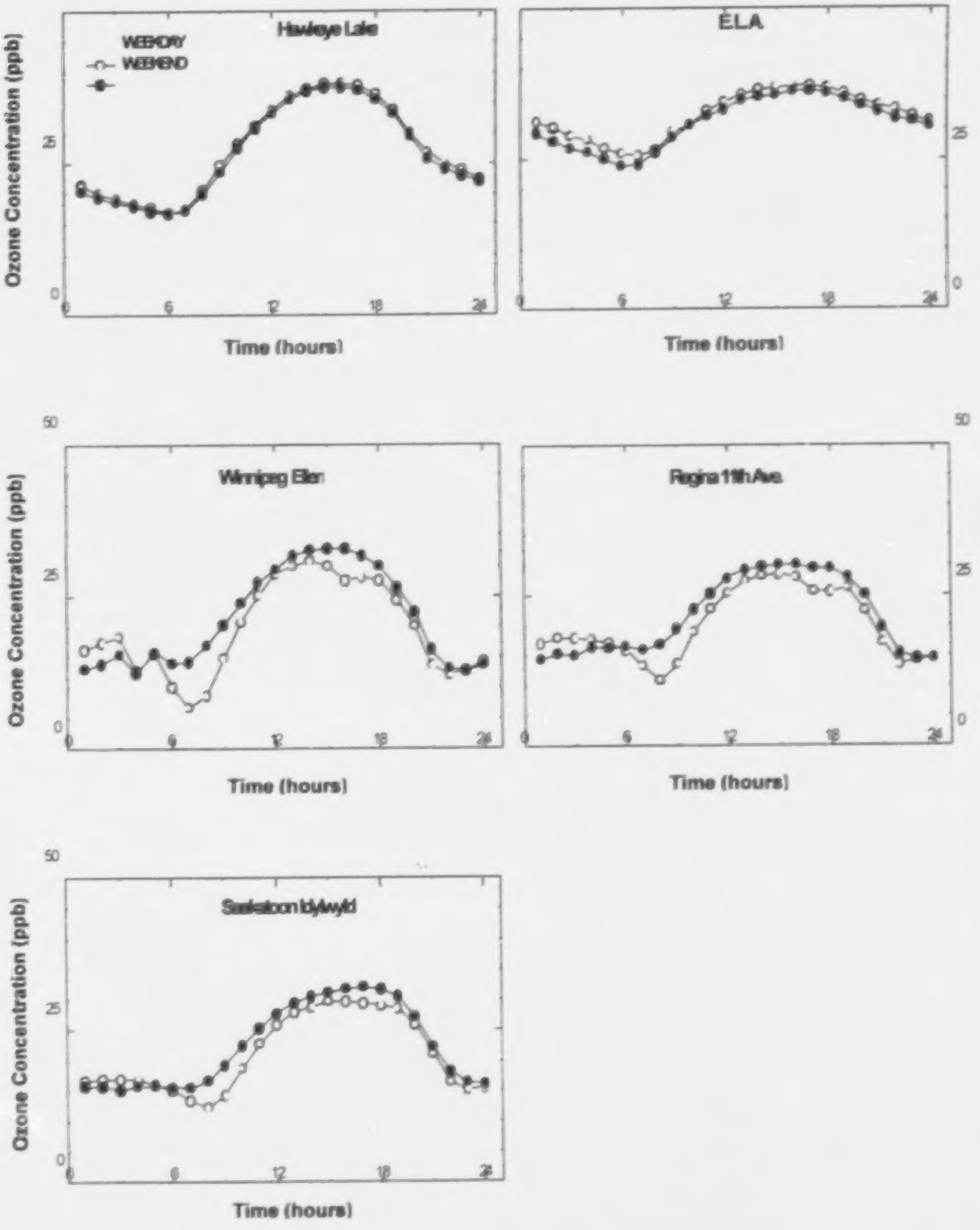


Figure 5.14 Hourly Average Ozone Concentrations (ppb) for Weekdays and Weekends (May to September, 1986 to 1993) - Toronto and Southern Ontario

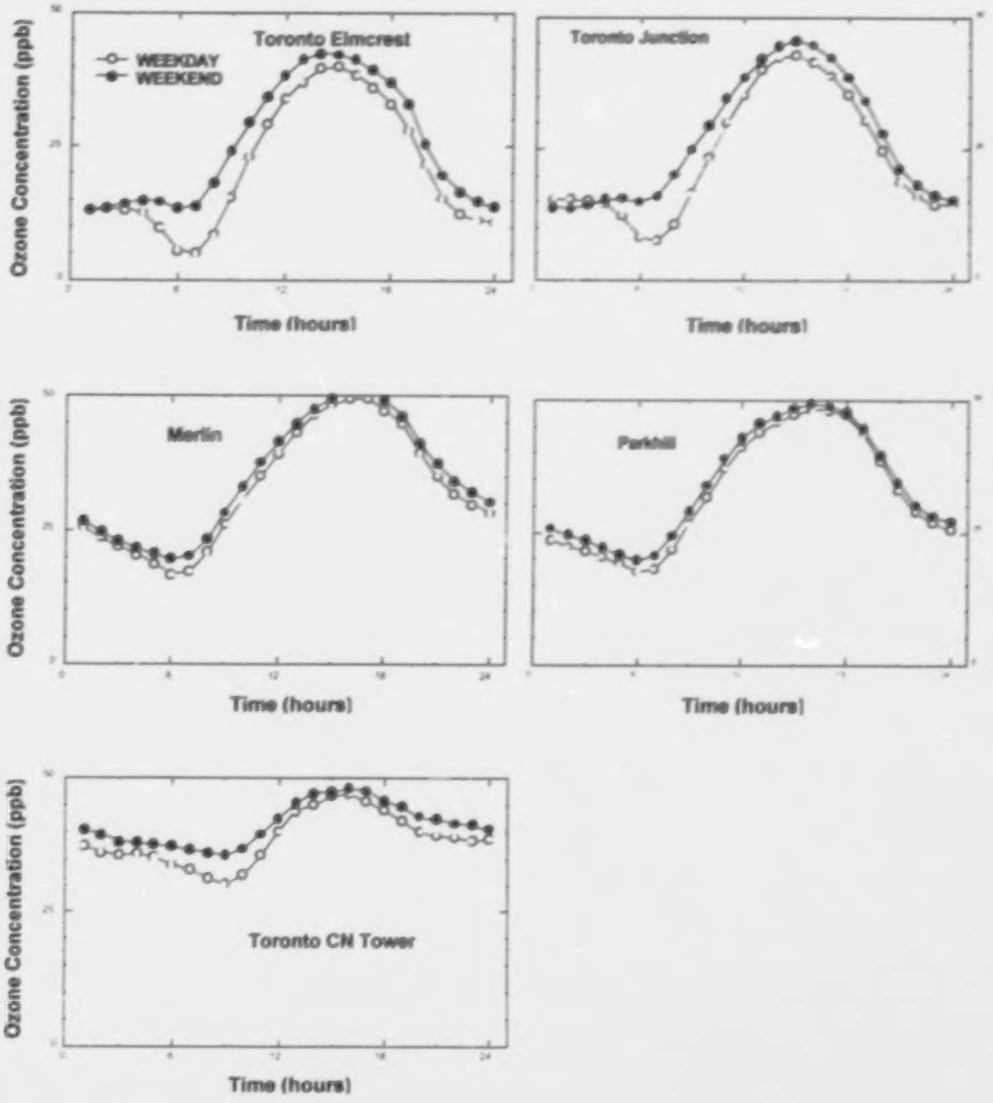
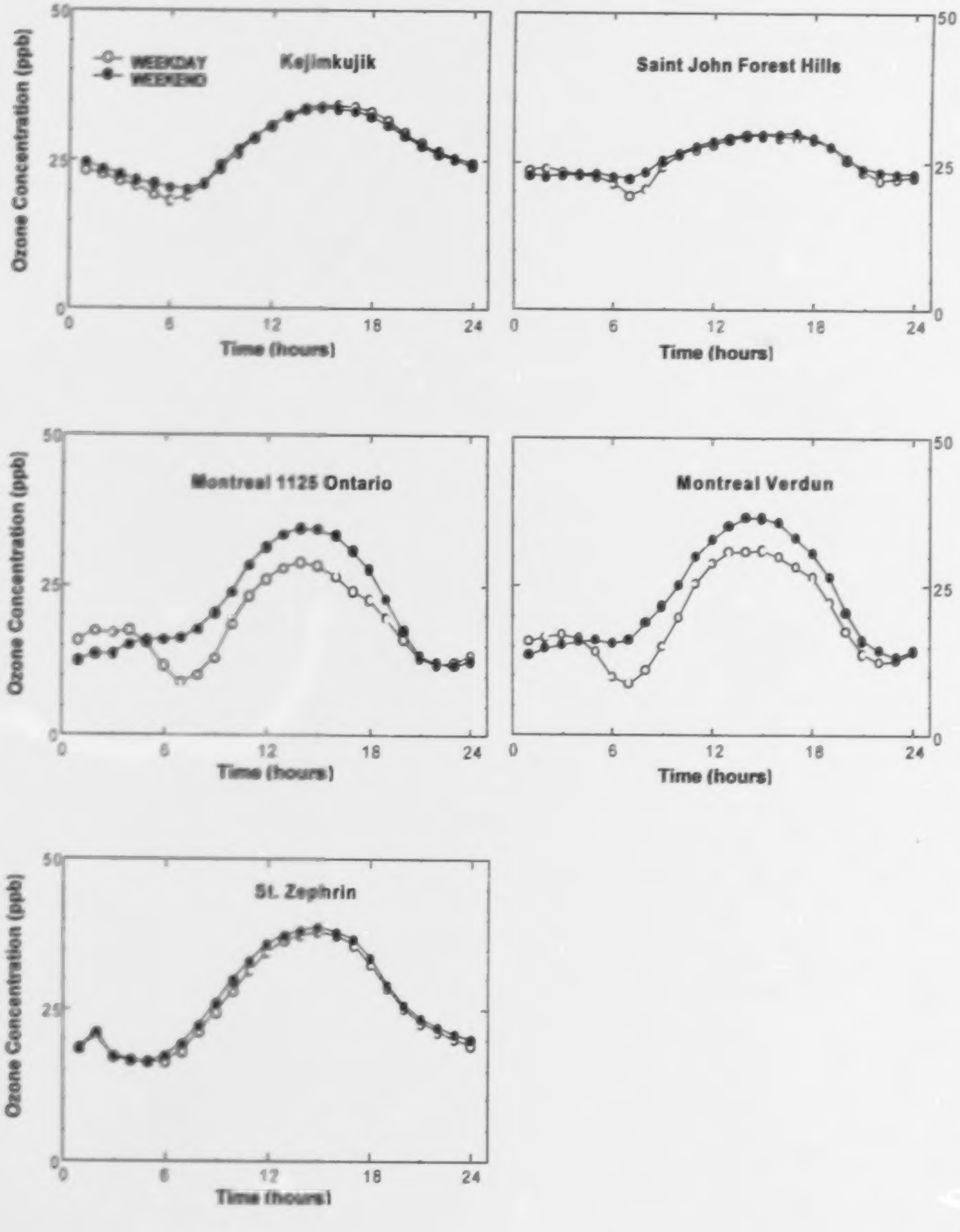


Figure 5.15 Hourly Average Ozone Concentrations (ppb) for Weekdays and Weekends (May to September, 1986 to 1993) - Montréal and Southern Atlantic



5.4 Trend Analysis

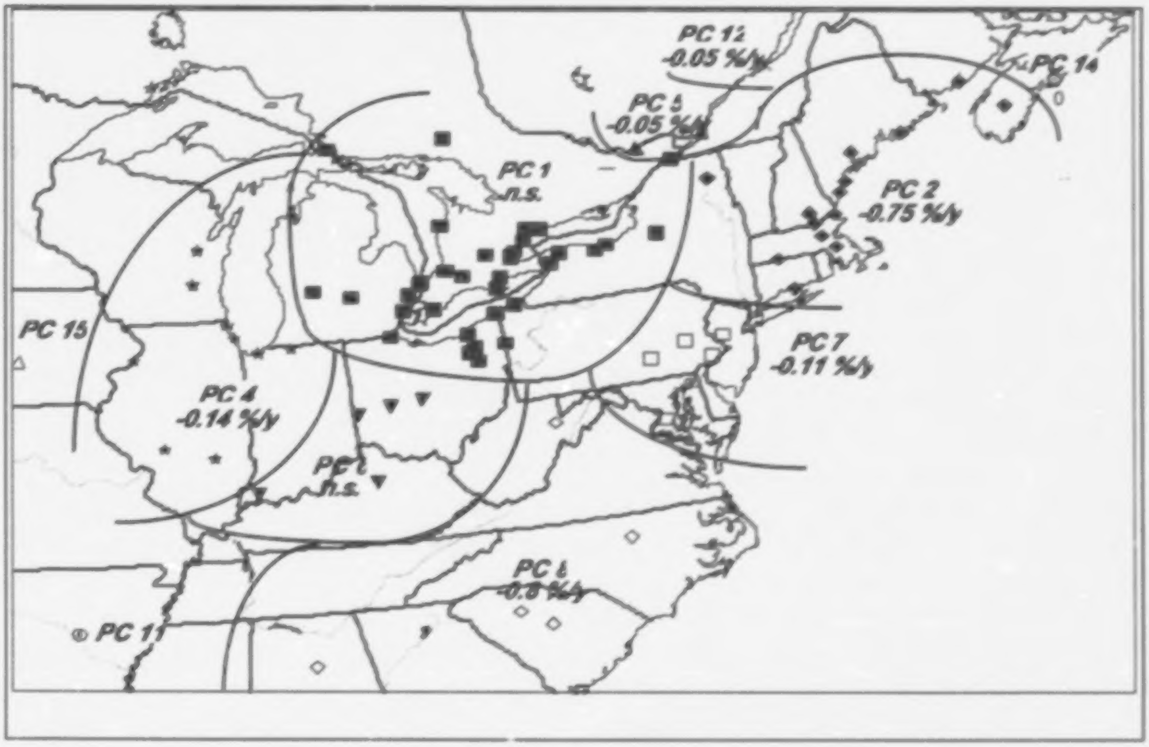
5.4.1 Principal Component Analysis and Trends in Mean and Daily Maximum Ozone

Most trend analyses for ozone have been carried out on single sites or for urban areas (Wakim, 1989; Jones et al., 1989; Curran & Frank, 1990; Dann, 1990; Fuentes & Dann, 1993). Since ozone episodes occur on a regional scale, this is a useful unit upon which to carry out the ozone trend analysis. As shown by Eder et al. (1993), principal component analysis (PCA) can be effectively used to study the regionality of ozone concentrations. In effect, PCA breaks apart regional concentrations of ozone levels by exploiting the correlation structure of the data. The analysis extended over the summer months (May to Sept.; 153 days) from 1985 to 1993.

Only Vancouver's Lower Fraser Valley (LFV), southern Ontario and southern Québec (mainly the Montréal area) have a sufficiently dense distribution of ozone monitoring stations to allow spatial analyses. The use of U.S. rural sites allows the spatial analysis to be extended to include most of northeastern North America. The PCA analysis therefore included both Canadian and U.S. monitoring sites. The PCA analysis did cluster sites within specific geographic sub-regions. These sub-regions were consistent with current knowledge of emission sources and of meteorological and topographical influences on ozone concentrations.

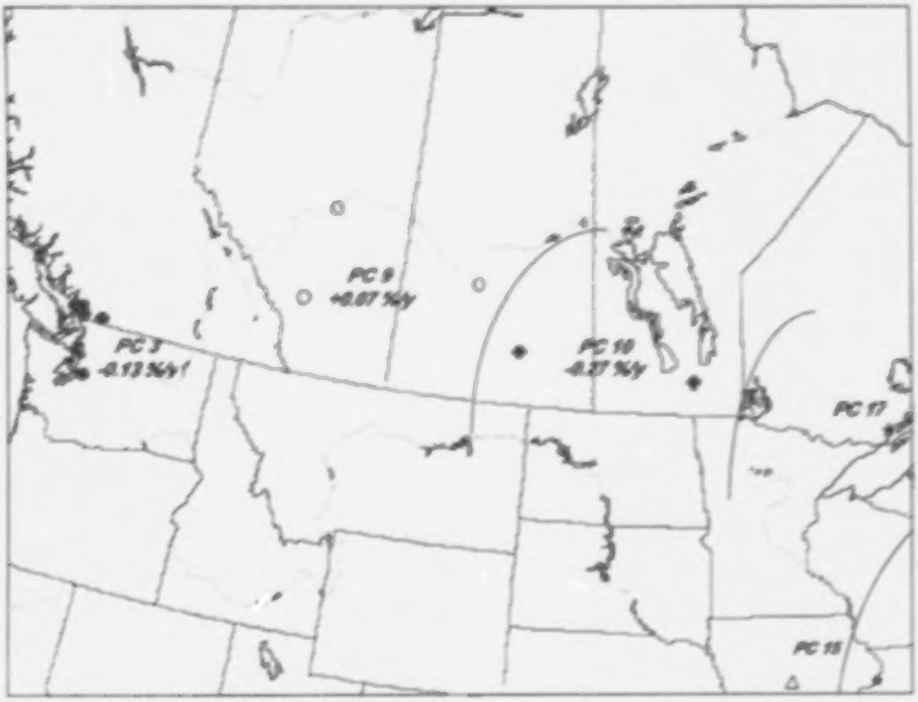
With only a few exceptions, the defined sub-regions incorporate the same set of stations whether the analysis is based on the daily mean or the daily maximum. Figure 5.16 shows the location of sites by sub-region for eastern North America and Figure 5.17 shows the location of sub-regions for the western sites (daily maxima analysis only).

Figure 5.16 Site Clusters Based on Daily Maximum Ozone for May-Sept. 1986 to 1993 - Eastern North America



PC 12
-0.05 %/y
PC 14
PC 5
-0.05 %/y
PC 1
n.s.
PC 2
-0.75 %/y
PC 15
PC 7
-0.11 %/y
PC 4
-0.14 %/y
PC 6
n.s.
PC 8
-0.8 %/y
PC 11

Figure 5.17 Site Clusters Based on Daily Maximum Ozone for May-Sept. 1986 to 1993 - Western North America



Most sub-regions showed a declining trend in daily maximum ozone ranging from 0.05%/yr. to 0.80%/yr. (significant at the 95% confidence level). PC1 (Southern Ontario/Great Lakes) showed no significant trend and one sub-region, PC9 (Saskatchewan/Alberta), showed an increasing trend of 0.07%/yr. The Iowa site also showed an increasing trend of 0.59%/yr. For the daily mean analysis, three sub-regions showed an increasing trend, ten a declining trend and one region no significant trend (no data shown here; refer to Report of the Data Analysis Working Group (Multistakeholder NO$_x$/VOC Science Program, 1997). An earlier analysis (Kim & Fuentes, 1995, 1996) for the 1982-93 time period (all months included) had indicated increasing trends in daily mean ozone in five out of ten regions. Eder et al. (1993) found no significant trend in mean or daily maximum ozone in identified sub-regions (U.S. data only) between 1985 and 1990.

5.4.2 Trends in Daily Maximum Ozone—Meteorologically Adjusted

The number, duration and intensity of summer ozone episodes at a given site are related in a complex manner to a variety of factors. These include precursor emission levels, solar radiation intensity, temperature and synoptic variables controlling air mass transport over medium and long-range spatial scales. Due to the strong correlation between meteorology and ozone concentrations, variations in meteorological conditions (on all time scales) not only have substantial impacts on ozone concentrations, but they are likely to mask any long-term trends in ozone that may be due to changes in emissions of NO_x and VOC (U.S. National Research Council (NRC), 1991). Accordingly, temporal changes in meteorological conditions need to be considered when assessing ozone trends and relating them to changes in precursor emissions.

Xu et al. (1995) have determined meteorologically adjusted trends for daily maximum ozone for the period 1980 to 1990 for a number of sites in southern Ontario and in Montréal. The trend analysis was recently extended to include sites in the Lower Fraser Valley and in the Southern Atlantic region for the period 1985 to 1992. Two regression modelling approaches were applied: Model 1 (with no meteorological parameters) took into account only a linear trend and seasonal variations; while Model 2 included the meteorological adjustment.

Windsor–Québec City Corridor

The results for locations in Ontario for the years 1980 to 1990 are presented in Table 5.4. The meteorologically adjusted trends for each site are given in column 2. The last column indicates the difference between Models 1 and 2 in terms of the yearly percentage change in ozone. On average, the use of a meteorological adjustment added a negative change of 0.3%/yr. to the base ozone trends. The adjusted trends show that annual change in daily maximum ozone varies from -0.7%/yr. (Ottawa) to +2.9%/yr. (Sudbury). While the overall trend appears to be that the ozone concentrations are increasing at a rate of 1.2%/yr., three sites show weak declining trends and a fourth site indicates no significant trend.

The results for three Québec sites are also shown in Table 5.4 for the years 1981 to 1993. Two sites have a declining trend of 1.5 and 1.1%/yr., while the third site indicates no significant change over the period. The use of a meteorological adjustment added a negative change of 0.4%/yr. to the base ozone trends. This was essentially the same effect found for the Ontario sites.

Lower Fraser Valley

Meteorologically adjusted trends for ten sites in Vancouver and the Lower Fraser Valley were computed for the period 1985 to 1992, as shown in Table 5.5. Seven sites indicated an increasing trend, while a declining trend is noted for the remaining three sites. The adjusted rates range from -1.3 to +1.7%/yr. For all sites, ozone is increasing at an average of 0.5%/yr. Differences in trends between Model 1 and 2 range from 0.2 to 0.2%/yr., with an average of 0.1%/yr.

Table 5.4 Trends in Daily Maximum Ozone for Ontario and Québec Sites with Meteorological Adjustment

Site	Trend from Model 2 %/yr.	Standard Error	T test value for slope = 0	Sign.	Δβ %/yr.
Ontario (1980-90)					
Burlington	1.1	0.0017	6.58	0.0001	0.2
Etobicoke	2.3	0.0020	11.27	0.0001	0.5
Kitchener	0.0	0.0020	0.20	0.8448	0.5
London	0.8	0.0015	5.11	0.0001	0.3
Ottawa	-0.7	0.0018	-3.69	0.0002	0.0
Sarnia	-0.1	0.0016	-0.77	0.4426	0.1
Stouffville	2.5	0.0016	15.49	0.0001	0.3
Sudbury	2.9	0.0029	10.08	0.0001	0.4
Tiverton	2.3	0.0018	13.11	0.0001	0.4
Toronto	2.5	0.0021	12.03	0.0001	0.5
Windsor	-0.6	0.0018	-3.55	0.0004	0.5
Region	**1.2**				**0.34**
Montréal (1981-93)					
Dorval	-1.5	0.0024	-6.37	0.0001	0.5
Pte. aux Trembles	0.0	0.0027	0.064	0.9491	0.4
Peel St.	-1.1	0.0037	-2.97	0.0030	0.2
Region	**-0.87**				**0.37**

Δβ=β1−β2 is the difference of trend between model 1 (no meteorological parameters) and 2 (meteorological parameters added).

Southern Atlantic Region

Similar variability is noted in the adjusted trends for the Southern Atlantic region based on the results from three sites (Table 5.5). The results show strong increasing trends at two sites and a strong declining trend at the third site. Values range from -3.7 to +7.5%/yr., while the composite trend averages 2.2%/yr. Differences in trends between Models 1 and 2 range from 0.3 to 0.4%/yr., with an average of 0.33%/yr.

Table 5.5 Trends in Daily Maximum Ozone for LFV and S. Atlantic Sites with Meteorological Adjustment

Site	Trend from Model 2 %/yr.	Standard Error	T test value for slope = 0	Sign.	Δβ %/yr.
LFV (1985-92)					
70th Ave.	1.3	0.0039	3.30	0.0010	-0.1
Hastings	1.1	0.0035	3.17	0.0015	0.1
Rocky Pt. Park	-0.7	0.0036	-2.05	0.0406	-0.1
Willingdon	-1.0	0.0033	-3.01	0.0027	0.0
Riverside Dr.	1.1	0.0041	2.72	0.0064	0.0
Sunnyside Rd.	1.5	0.0034	4.40	0.0001	-0.2
Welsh Rd.	0.2	0.0050	0.46	0.6427	0.2
Ring Rd.	1.7	0.0031	5.66	0.0001	-0.1
72nd Ave.	-1.3	0.0034	-4.13	0.0001	-0.2
Abbotsford	0.6	0.0031	1.93	0.0540	-0.2
Region	**0.45**				**-0.06**
Atlantic (1985-92)					
Shearwater	7.5	0.0036	21.225	0.0001	0.3
Saint John (P.O.)	2.8	0.0040	6.866	0.0001	0.4
Saint John (FH)	-3.7	0.0038	-9.853	0.0001	0.3
Region	**2.2**				**0.33**

$\Delta\beta = \beta 1 - \beta 2$ is the difference of trend between models 1 (no meteorological parameters) and 2 (meteorological parameters added).

5.4.3 Summary

The application of the regression model to daily maximum ozone levels at selected urban sites in the three regions revealed strong inconsistencies in the trends within each region. The aggregate values suggest an increasing trend for urban areas within each of the regions. The decrease of NO levels at many urban sites with a resulting decrease in ozone scavenging is the most apparent reason for the increase in average daily maximum ozone concentrations.

5.5 OZONE ANALYSIS FOR AN 8 HOUR AVERAGING PERIOD

The analysis presented in this section is based upon the Report to the Health Objective Working Group - Ozone Data Analysis for Six and Eight Hour Averages (1980 - 1992) (Dann, 1994). Only the 8 hour data are discussed here. Ozone data were extracted from the NAPS database for the period 1980 to 1992, and results are reported for 35 sites in five regions most impacted by ozone - Southern Atlantic, Montréal, Toronto/Hamilton/Niagara, Southwestern Ontario and Vancouver and for six remote (background) sites (first 6 sites in Table 5.6). Sites were chosen based on completeness of data record and representativeness of the site within the region (Fuentes and Dann, 1993). The remote sites had a much shorter data record than the other sites but are useful for comparison purposes. Running averages were based on end time (i.e. the running eight hour average for 01:00 on day 2 represents the period 17:00 on day 1 to 01:00 on day 2). A seventy-five percent data completeness requirement was used to calculate a valid eight hour running average.

5.5.1 Frequency of Daily Maximum 8 Hour Ozone Concentrations

The percentile distributions for daily maximum eight-hour ozone concentrations at 41 Canadian sites are provided in Table 5.6 for the period 1980 to 1992. The percentiles show the percentage of days with daily maxima equal to or less than the indicated value.

Table 5.6: Frequency distribution of daily maximum 8 hour running averages - 1980 - 1992

8 hr Running Average							Percentiles												
Station	City	Address	Start	Stop	Days	Min	5	10	25	50	75	90	95	98	99	99.9	Max.	Mean	Std. Dev.
10201	CORMACK, NFLD.	CORMACK	4/19/1989	12/21/1992	862	7	19	21	25	31	38	45	49	51	55	61	61	32.1	9.3
54001	MONTMORENCY, QUÉBEC		5/31/1988	12/30/1992	1558	7	21	25	29	34	40	49	54	63	71	89	91	35.7	10.5
54101	SUTTON, QUÉBEC		12/6/1988	5/31/1990	366	9	19	23	28	34	44	53	59	66	73	77	77	36.2	12.0
54201	CHAPAIS, QUÉBEC		6/10/1988	5/31/1990	685	9	20	24	28	34	42	50	56	63	67	87	87	35.4	11.0
64001	ELA, ONT.	EXPERIMENTAL LAKES AREA	5/9/1988	12/30/1992	1419	14	23	26	30	36	44	51	56	61	64	75	76	37.3	10.1
102001	SATURNA, B.C.		5/28/1991	12/30/1992	579	6	19	22	27	32	38	45	48	52	57	66	66	32.8	9.1
30501	KEJIMKUJIK, N.S.	NATIONAL PARK	4/16/1985	12/31/1991	2311	9	20	22	27	32	39	47	55	65	73	97	103	34.0	11.3
40202	SAINT JOHN, N.B.	POST OFFICE	1/1/1980	10/15/1991	3778	1	13	17	23	30	39	48	57	68	75	121	135	31.5	13.8
40203	SAINT JOHN, N.B.	FOREST HILLS	1/1/1980	12/31/1992	4247	2	14	18	24	31	41	50	59	73	86	134	146	34.0	15.0
40501	POINT LEPREAU, N.B.	MAIN GATE	7/15/1986	11/29/1992	1005	1	10	20	27	34	43	58	71	88	95	120	135	36.9	17.6
50102	MONTRÉAL, QUÉBEC	JARDIN BOTANIQUE	1/1/1980	10/17/1992	3829	1	6	9	14	23	33	44	54	64	73	99	106	25.0	14.8
50103	MONTRÉAL, QUÉBEC	POINTE-AUX-TREMBLES	1/1/1980	10/31/1992	3868	1	8	10	17	25	34	45	54	63	71	94	146	26.6	14.3
50104	MONTRÉAL, QUÉBEC	1125 ONTARIO EST	1/1/1980	12/31/1992	4215	1	5	8	13	20	30	44	54	66	75	98	106	23.6	15.1
50110	MONTRÉAL, QUÉBEC	PARC PILON, MTL.-NORD	3/7/1980	12/31/1992	3765	1	5	9	15	23	33	46	58	71	80	114	121	25.6	16.3
50112	MONTRÉAL, QUÉBEC	BOUL. LAURENTIDES	1/1/1980	9/30/1992	3793	1	8	10	18	26	36	48	59	71	80	108	125	28.1	15.9
50113	MONTRÉAL, QUÉBEC	PIE X & CARDINAL	1/1/1980	9/30/1992	3961	1	9	11	20	29	39	50	61	75	85	115	123	30.3	16.4
60204	WINDSOR, ONT.	467 UNIVERSITY AVE. WEST	1/1/1980	12/31/1992	4653	0	6	9	15	26	43	61	72	83	90	109	135	30.9	20.6
61004	SARNIA, ONT.	FRONT ST. AT C.N. TRACKS	1/1/1980	12/31/1992	4712	1	10	15	23	31	42	57	68	79	87	103	128	33.6	17.1
61005	SARNIA, ONT.	MTC SHED	1/1/1980	12/31/1992	4433	1	14	17	24	32	44	60	71	83	92	111	130	35.6	17.5
62101	HURON PARK, ONT.	COLLEGE OF AGRICULTURE	1/1/1980	11/9/1991	3981	3	15	19	25	33	45	61	71	82	88	109	116	36.5	17.1
62201	MERLIN, ONT.	MOE WATER PUMP STN.	1/1/1980	12/31/1992	4561	0	14	18	24	32	45	61	72	83	92	115	125	36.2	17.7
62401	PARKHILL, ONT.	PUC BLDG	7/22/1983	12/31/1992	3246	1	15	18	26	34	47	64	74	87	94	115	120	38.1	18.1

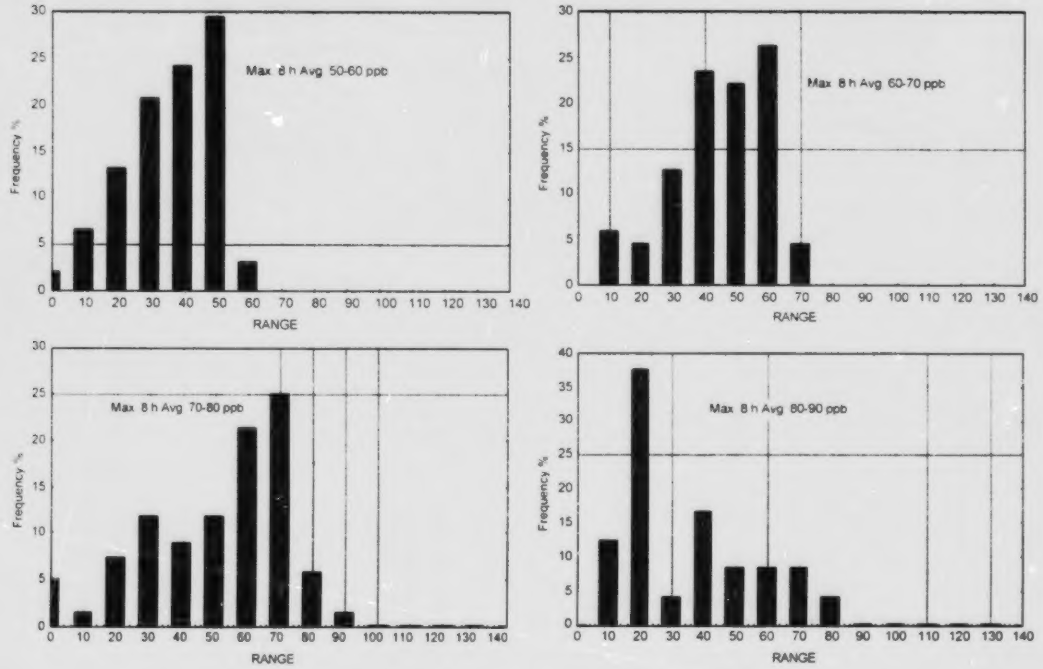
8 hr Running Average

Station	City	Address	Start	Stop	Days	Min	Percentiles										Max	Mean	Std. Dev.
							5	10	25	50	75	90	95	98	99	99.9			
62501	TIVERTON, ONT	CON. RD. 2 LOT A	1/1/1980	12/31/1992	4538	1	20	24	30	36	47	64	76	90	98	121	139	40.4	17.0
62601	SIMCOE, ONT	EXPERIMENTAL FARM	1/1/1980	12/31/1992	4524	1	17	21	27	36	49	65	76	86	93	110	172	39.7	18.1
60413	TORONTO, ONT.	ELMCREST ROAD	1/1/1980	12/31/1992	4506	0	6	10	17	25	38	53	66	80	88	110	117	28.9	18.1
60415	TORONTO, ONT	QUEENSWAY W & HURONTARIO	1/1/1980	12/31/1992	4567	0	7	10	16	24	35	49	60	73	82	113	138	27.2	16.6
60418	TORONTO, ONT	JUNCTION TRIANGLE	3/20/1981	12/31/1992	4167	0	6	10	17	26	38	53	66	79	86	110	134	29.5	17.9
60513	HAMILTON, ONT	VICKERS RD. & EAST 18TH ST	10/10/1985	12/31/1992	2569	0	8	11	18	27	41	59	69	80	87	107	115	31.4	18.6
61302	ST. CATHARINES, ONT	ARGYLE CRESCENT	1/5/1988	12/31/1992	1737	1	12	15	21	30	43	59	69	78	83	102	125	33.8	17.4
61602	OAKVILLE, ONT	BRONTE RD. & WOBURN CRES	4/9/1980	12/31/1992	4531	0	10	14	20	29	41	54	65	76	84	108	140	32.0	16.8
61701	OSHAWA, ONT	RITSON RD. & OLIVE AVE	1/1/1980	12/31/1992	4595	0	9	13	19	27	36	48	60	76	86	103	140	29.2	15.6
62901	NIAGARA FALLS, ONT	ALLENDALE AVE	5/18/1988	12/31/1991	1285	1	13	17	24	34	50	68	78	90	96	127	127	38.4	20.2
100108	VANCOUVER, B.C	250 WEST 70TH AVENUE	1/1/1980	12/31/1992	4094	0	2	4	10	19	28	34	39	43	48	65	92	19.4	11.6
100111	VANCOUVER, B.C	ROCKY PT. PARK	1/1/1980	12/31/1992	4337	0	2	5	12	24	35	46	55	68	77	121	159	25.2	17.1
100122	VANCOUVER, B.C	SUNNYSIDE ROAD ANMORE	5/1/1982	12/31/1992	3594	0	7	11	18	26	34	43	50	62	71	111	140	26.9	13.8
100124	VANCOUVER, B.C	475 GUILDFORD WAY PORT MOODY	5/1/1982	12/31/1992	2893	0	2	4	12	21	31	40	46	57	67	87	109	22.4	14.2
100126	VANCOUVER, B.C	RING ROAD BURNABY	6/1/1984	12/31/1992	2770	2	12	15	20	25	32	39	45	54	60	88	124	26.6	10.6
100127	VANCOUVER, B.C	19000 & 72ND AVE. SURREY	12/22/1983	12/31/1992	3105	0	6	10	19	28	36	44	50	58	66	90	100	28.1	13.6
100129	VANCOUVER, B.C	HAMILTON & PAISLEY	6/8/1987	12/31/1992	1577	0	5	10	18	26	35	43	49	58	70	102	119	26.7	13.6
101001	ABBOTSFORD, B.C	AIRPORT	8/1/1982	1/3/1992	3008	0	7	12	22	31	39	47	54	62	70	88	107	30.5	14.0
101201	PITT MEADOWS, B.C	AIRPORT	5/21/1985	12/31/1992	2166	0	4	8	18	26	35	44	50	58	66	80	99	26.8	13.8

5.5.2 Partitioning of Hourly Data for Selected Daily 8 Hour Maxima

Counts of hourly averages within 10 ppb concentration classes from 0-200 ppb were determined for daily maximum 8 h concentrations over the range of 50 to 200 ppb. The results of this analysis for 41 sites are provided in detail in Dann, 1994. Figures 5.18 to 5.23 show the frequency distribution of hourly concentrations when eight hour daily maxima were in the range of 50 to 90 pbb for selected sites. These plots are provided by region for the year 1988 (a high ozone year). The x-axis numbers represent the start values of the 10 ppb ranges (i.e. 50 represents 50-60 ppb). For any given 8 hour daily maximum concentration there is a very low probability of occurrence of hourly maxima that are 20 ppb or more greater than the 8 hour daily maximum concentration. This is also illustrated in Figure 5.24 which shows the relationship between daily maximum one hour concentrations and daily maximum eight hour concentrations for 1992. Analyses of data from other years show similar regressions to that in Figure 5.24. The graphs were constructed using all days with one hour ozone maximum > 50 ppb for all 41 sites.

Figure 5.18: Frequency of hourly averages for selected daily 8 hr maximum ozone concentrations (ppb) - Remote sites 1988. X-axis values represent the starting value for each 10 ppb range.



F2

Figure 5.19: Frequency of hourly averages for selected daily 8 hr maximum ozone concentrations (ppb) - Southern Atlantic Region 1988. X-axis values represent the starting value for each 10 ppb range.

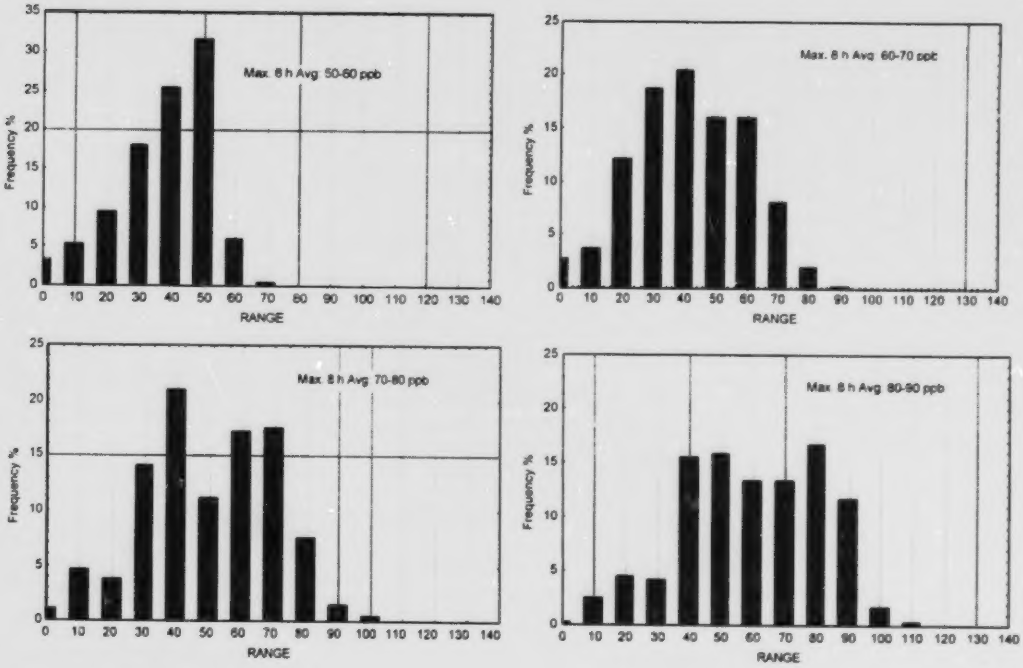


Figure 5.20: Frequency of Hourly Averages for Selected Daily 8 h Maximum Ozone Concentrations. (ppb) - Montréal 1988.. X-axis values represent the starting value for each 10 ppb range.

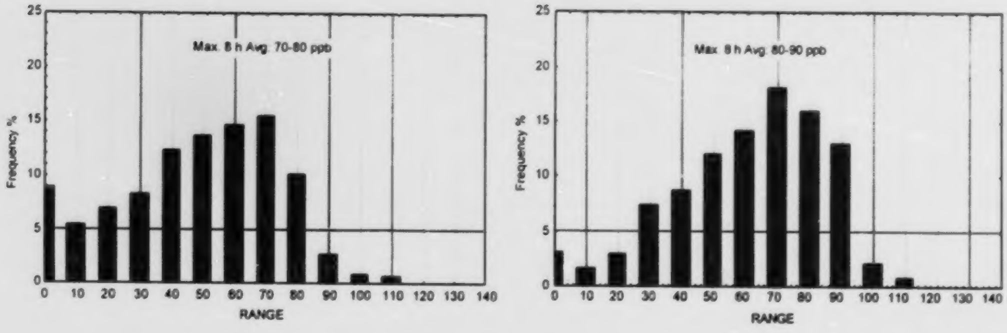


Figure 5.21: Frequency of hourly averages for selected daily 8 hour maximum ozone concentrations (ppb) - Southwestern Ontario 1988. X-axis values represent the starting value for each 10 ppb range.

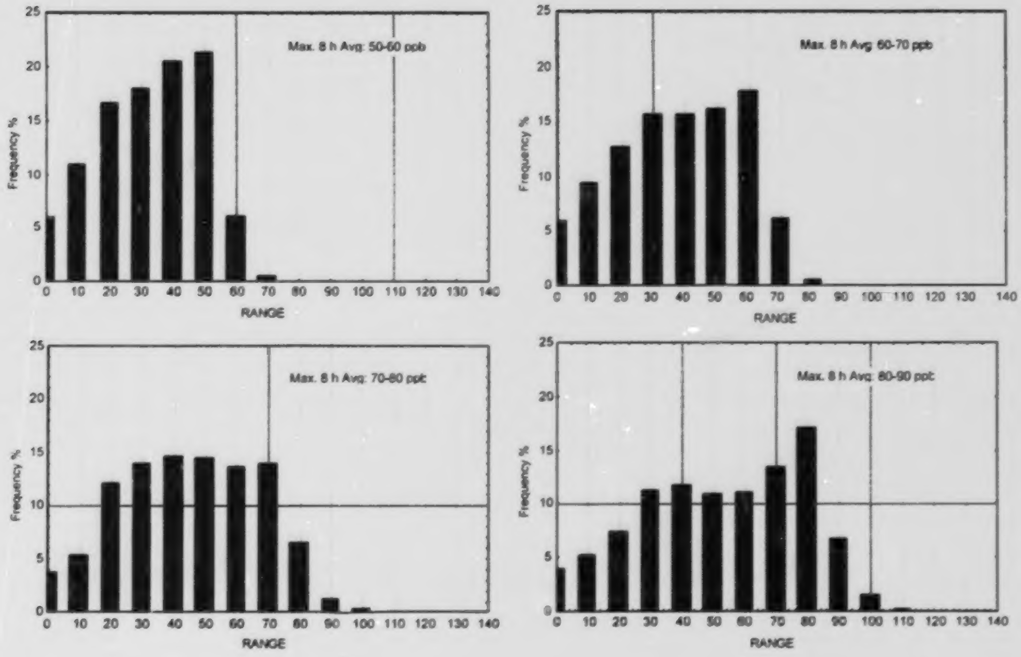


Figure 5.22: Frequency of hourly averages for selected daily 8 hr maximum ozone concentrations (ppb) - Toronto/Hamilton/Niagara 1988. X-axis values represent the starting value for each 10 ppb range.

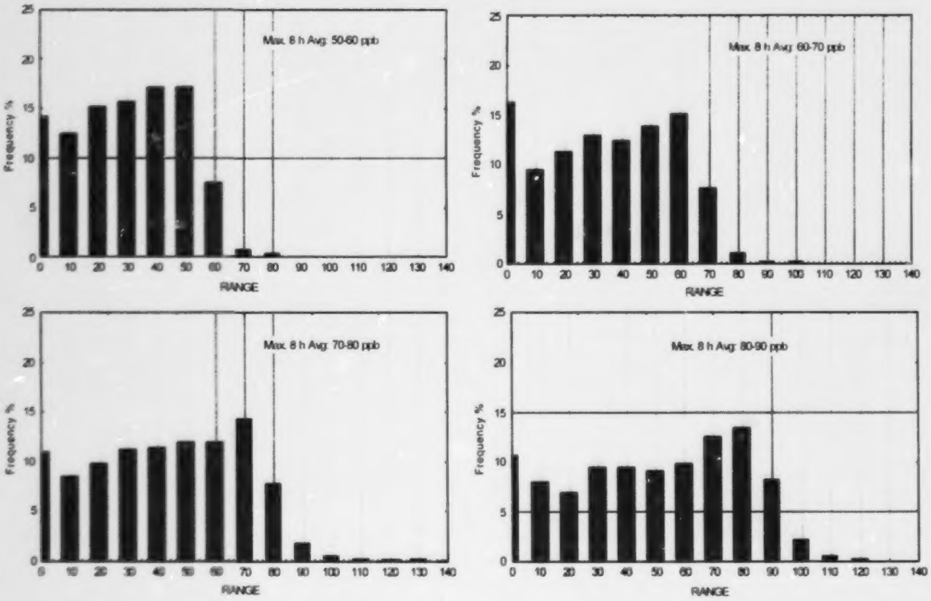


Figure 5.23: Frequency of hourly averages for selected daily 8 hour maximum ozone concentrations (ppb) - Vancouver / Lower Fraser Valley 1988. X-axis values represent the starting value for each 10 ppb range.

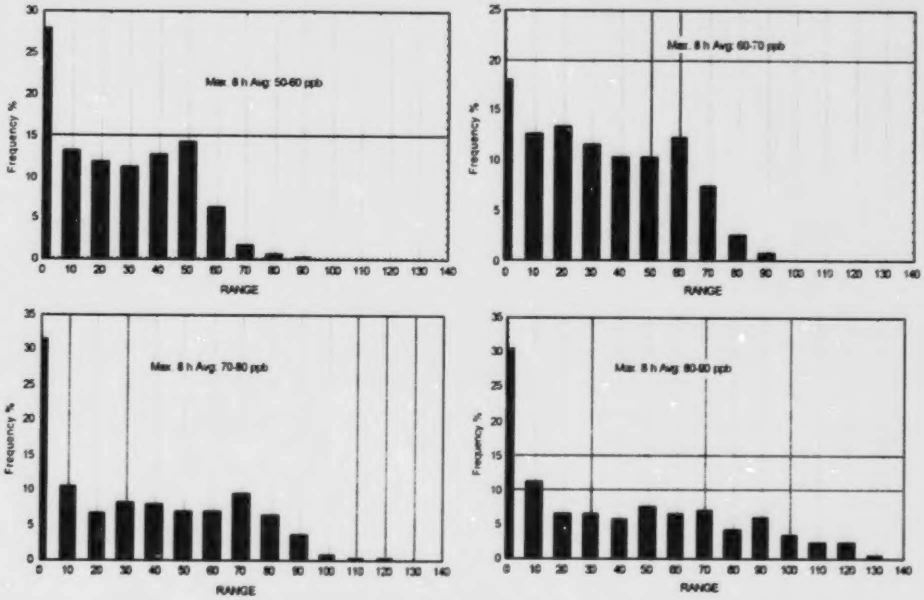
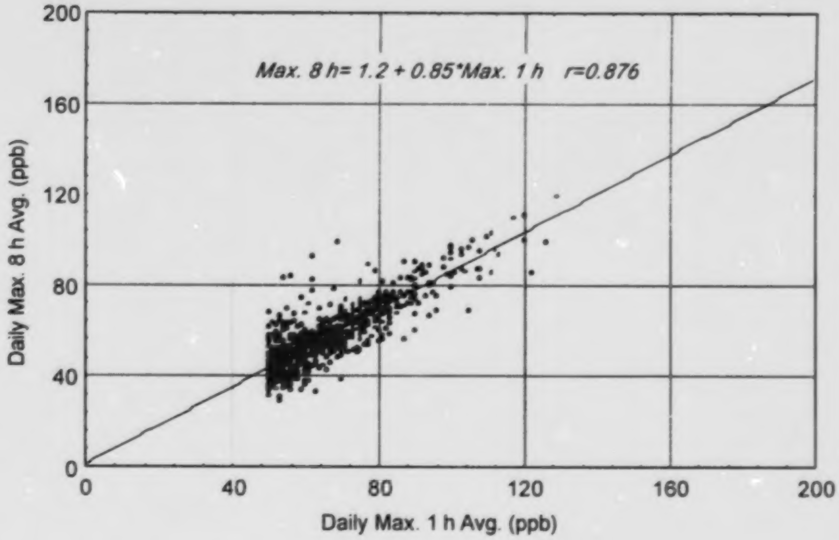


Figure 5.24: Relationship Between Daily Maximum 8 hour Average and Daily Maximum 1 hr. Avg. for 1992 – All Sites (n=1541)



5.5.3 Diurnal Patterns of 8 hour Average Ozone

An analysis of the time of day occurrence of running 8 hour average ozone concentration greater than selected values was also carried out (Dann, 1994). Sample outputs shown in Figures 5.25 to 5.27 are for counts of 8 hour running averages greater than 70 ppb by end time for each site group for the years 1988, 1990 and 1992 (high, moderate and low ozone years respectively). Running averages were based on end time (i.e.; the running eight-hour average for 01:00 on day 2 represents the period 17:00 on day 1 to 01:00 on day 2). The order of plotting has been changed on some of the graphs to improve legibility. Figures 5.28 and 5.29 show mean concentrations of 8 hour running average ozone by end time for periods greater than 70 ppb (remote sites not included because of very few occurrences of 8 hour ozone > 70 ppb). These figures display data for the year 1988 only.

At most sites the highest number of 8 hour averages greater than 70 ppb occurred somewhere between the 1000-1800 and 1300-2100 time periods (endtimes 18 to 21, Figures 5.25 – 5.27). The Montréal and southern Atlantic sites showed less diurnal variation in counts of running 8 hour averages greater than 70 ppb than the other non-remote sites. Remote sites, not surprisingly, had the fewest counts of running 8 hour averages greater than 70 ppb. Mean eight hour concentrations by end time (for 8 hour periods > 70 ppb) were very similar for all site groupings except southern Atlantic for end times between 1500 and 1900 (Figures 5.28 and 5.29). For other periods of the day there were large differences between regions.

Figure 5.25: Site average count of 8 hour running average ozone >70 ppb by end time - 1988.

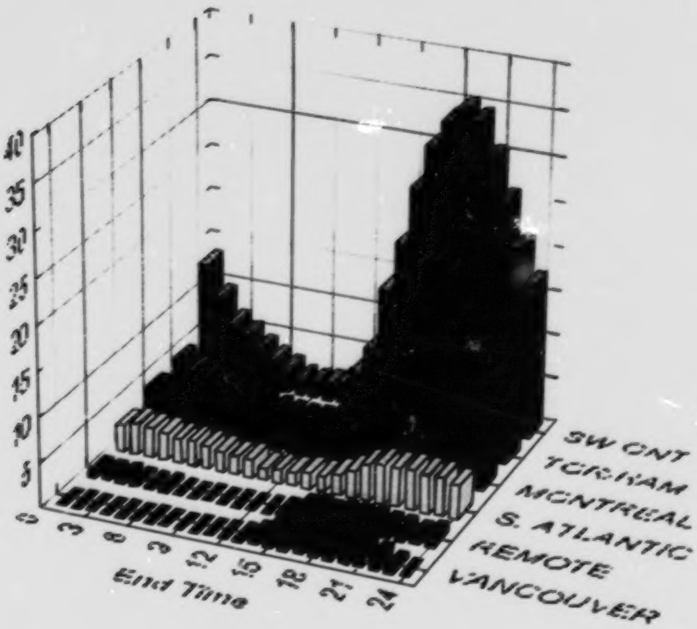


Figure 5.26: Site average count of 8 hr running average ozone >70 ppb by end time - 1990.

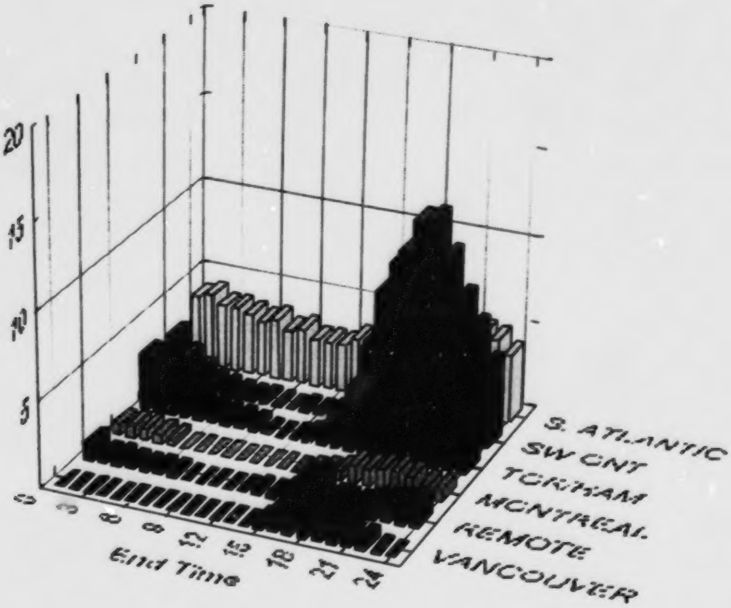


Figure 5.27: Site average count of 8 hr running average ozone >70 ppb by end time - 1992.

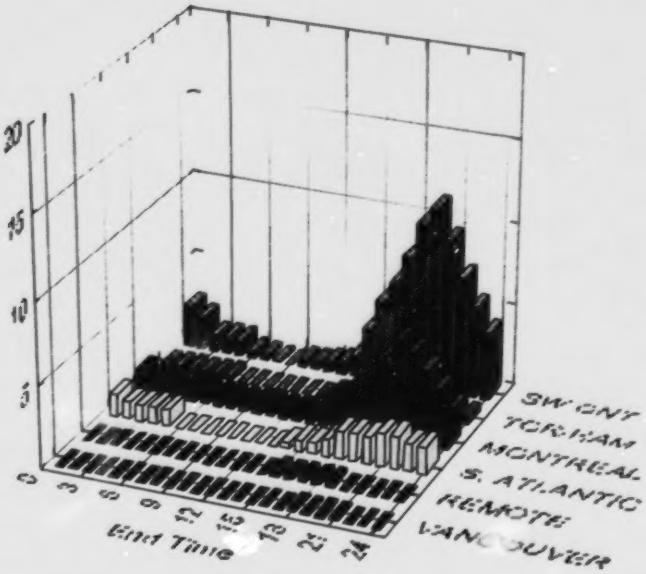


Figure 5.28: Mean 8 hr ozone concentration (ppb) by end time, 1988 (for 8 hr periods >70 ppb only) - Windsor / Québec City Corridor.

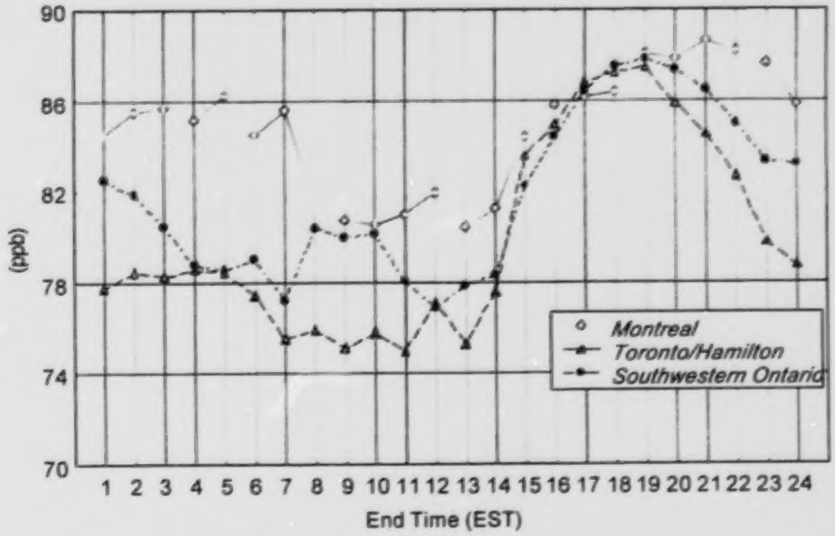
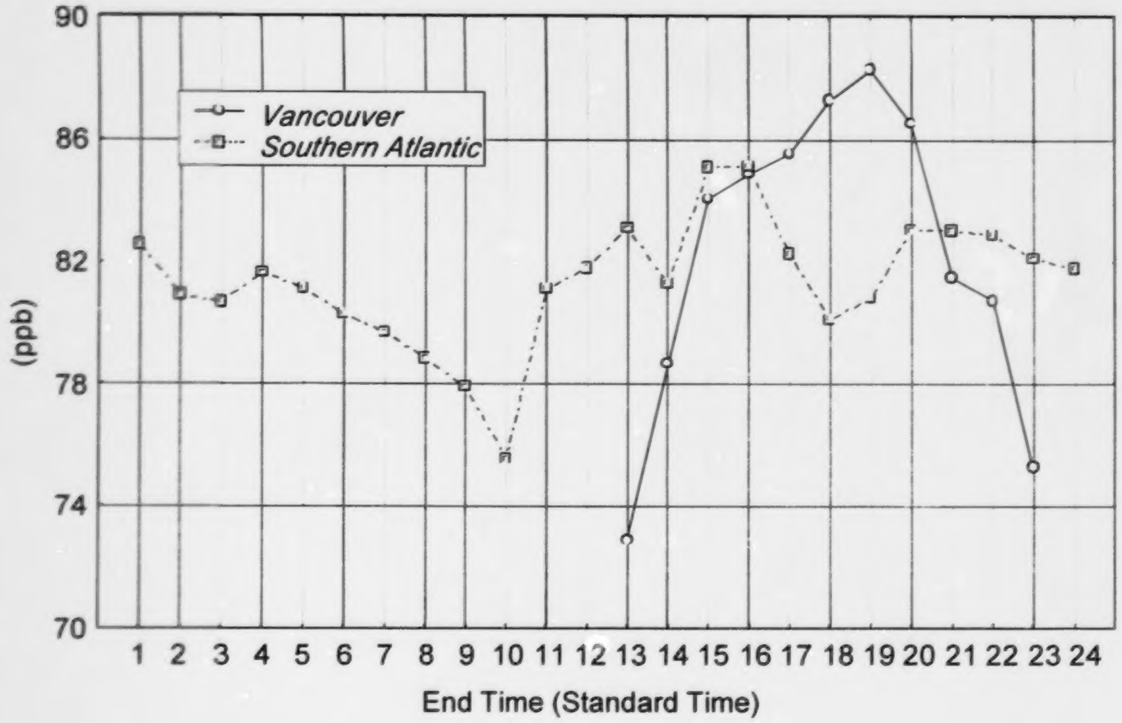


Figure 5.29: Mean 8 hour ozone concentrations (ppb) by end time, 1988 (for 8 hr periods >70 ppb only) - Vancouver and Southern Atlantic Region.



5.5.4 Summary of 8 hour ozone data

As described in Chapter 3 of this document, measurements of ambient ozone with modern continuous analyzers store ozone readings each minute. Data are generally reported over a 1 hour averaging time. The database of hourly ozone values at each site can, however, be easily converted to other ozone metrics. This section has presented an overview of ozone values for an 8 hour averaging period for different regions of Canada. The analysis has shown that for any given 8 hour daily maximum concentration, there is a very low probability that hourly maxima, 20 ppb or more greater than the 8 hour daily maximum concentration, will occur. Analyses of the time-of-day occurrence of high 8 hour values (> 70ppb) showed that these tended to occur between the 1000-1800 and 1300-2100 time periods.

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Environment Canada Environnement Canada

NATIONAL AMBIENT AIR QUALITY OBJECTIVES FOR GROUND-LEVEL OZONE

SCIENCE ASSESSMENT DOCUMENT

A Report by
the Federal-Provincial Working Group
on Air Quality Objectives
and Guidelines

July, 1999

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Part 3 of 7

Canada

6 ASSESSMENT OF EXPOSURE

This chapter discusses factors which influence human exposure to ozone and presents information on the relationships between ambient, indoor and personal[1] ozone levels. Estimates of the frequency of contact between the Canadian population and ozone through air were extrapolated from the results of modelling efforts for three urban areas in Canada. This assessment does not consider human exposure to ozone that occurs after ozone has transferred to another environmental medium (i.e. deposition into food, water or soil) because ozone's high reactivity makes exposure via another route unlikely.

6.1 CONCEPTS

Just as several factors influence outdoor ozone concentrations—photochemical production, long-range transport of non-locally produced ozone, intrusion from the stratosphere, and removal by scavenging—several factors influence individual exposure to ozone. *Exposure* is defined as any contact at a boundary (surface) between a target (who is being exposed) and a specific contaminant concentration for a specified time interval (National Research Council (NRC), 1991). For airborne contaminants, the boundary consists of the outer (skin) or inner (respiratory tract epithelium) surface of the body (Sexton & Ryan, 1988). The *dose* is defined as the measured or estimated exposure at the inner contact surface; that is, the actual amount of pollutant that enters the body and reaches the target tissue, in this case the respiratory system (Sexton & Ryan, 1988). In determining the likelihood of human health impacts, scientists require clarity when estimating dose and/or exposure, since the concentrations measured at the outer boundary may not equal those that reach the inner boundary. This assessment, therefore, focuses on the key extrinsic determinants of a response: magnitude (concentration), duration (length of time) and pattern of exposure, and the ventilation rate of the individual at the time of exposure (Hazucha, 1987; Silverman et al., 1976; United States Environmental Protection Agency (U.S. EPA), 1978, 1986, 1993).

The NO_x/VOC Management Plan states that "in summer months, more than half of all Canadians are routinely exposed to ambient air ozone concentrations that are known to cause adverse effects on health" (p. xii, Canadian Council of Ministers of the Environment (CCME), 1990). Although this statement includes an estimate of the size of the exposed population, it does not include observations or estimates of who is exposed, where, when or how often. Therefore, to determine the likelihood of human health impacts of ground-level ozone in Canada, scientists and policy-makers require better estimates of human exposure to ozone.

There are two ways of determining exposure: *directly* at the point at which it occurs—by providing each person with a personal monitor to carry for the period of the study; or it can also be *predicted*—using concentration, fate and distribution information combined with data (from time activity diaries and questionnaires) on activities which bring the individual in contact with the contaminant.

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[1] This is the ozone concentration experienced by an individual during normal daily acitivities.

6.2 DIRECT EXPOSURE ASSESSMENT

6.2.1 Personal Monitoring

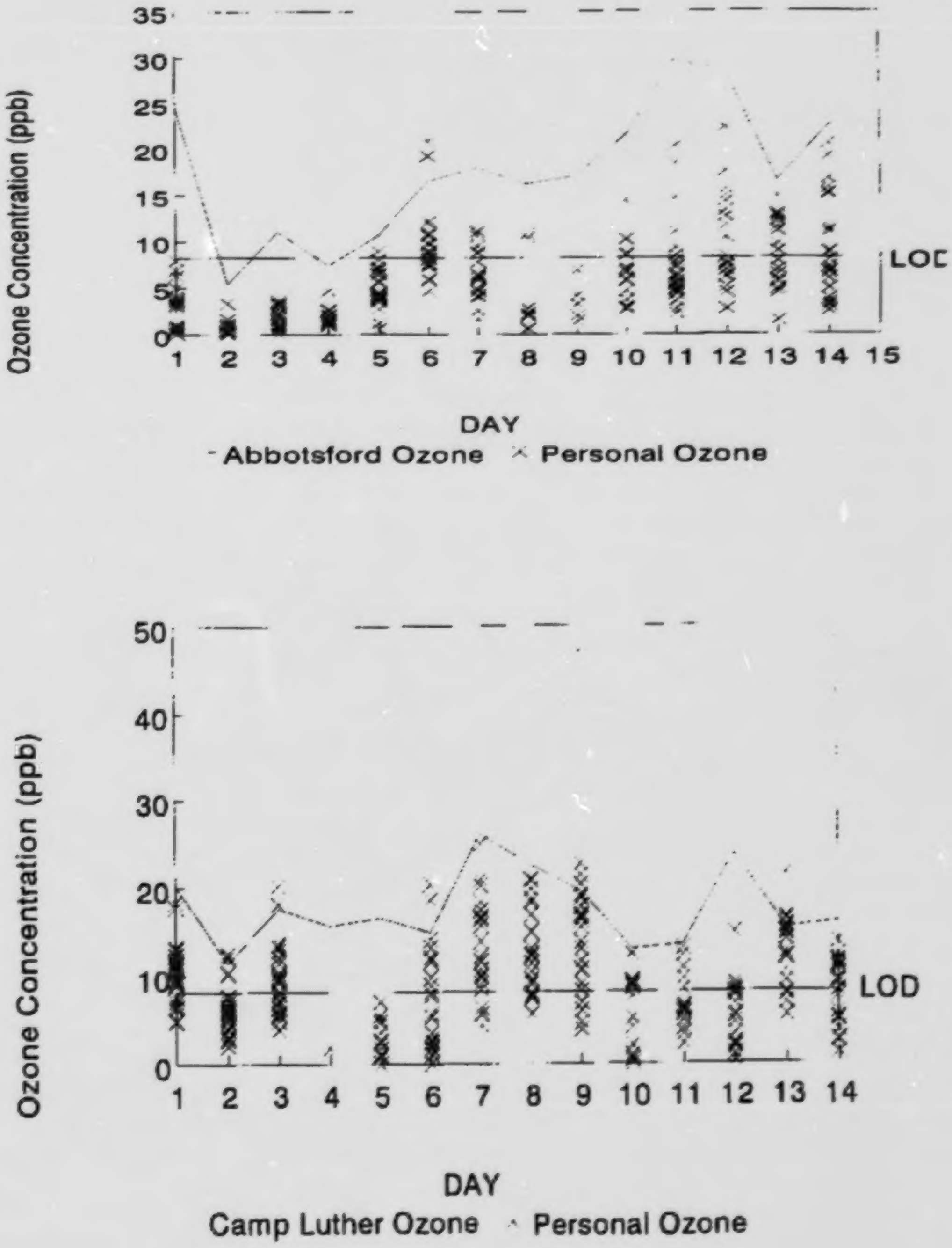
Brauer and Brook (1995) demonstrated the effects of time-activity patterns on personal ozone exposure during studies in the Lower Fraser Valley (LFV) during the summers of 1992 and 1993. They collected 14 days of personal samples (24-hour average) in the summer of 1992 from two groups of individuals: 25 Health Unit workers (Group 1) and 25 individuals from a Lutheran overnight camp (Group 2). Each participant recorded where they were (indoors, outdoors, in transit and in what location) for each hour of the day. In the summer of 1993, 15 adult farmworkers (Group 3) wore passive samplers during the work shift (6-14 hours) for 25 days. From Groups 1,2 and 3 respectively, the researchers collected 304, 287, and 219 valid personal ozone samples.

In addition, Brauer and Brook co-located passive samplers with continuous ozone analyzers at three fixed ambient monitor (FAM) sites: Pitt Meadows (Airport), Abbotsford in 1992, and Surrey in 1993. They also collected daily 24-hour passive samples (n=115) for 35 days. After calculating the passive monitor sampling rate, they compared the 24-hour average ozone concentrations from the passive sampler with the mean of the hourly average concentrations from the FAM. They found a good agreement between the samplers (r^2=0.75) as defined by the linear relationship: passive $[O_3]$ =0.95 × continuous $[O_3]$. The authors then used the monitor closest to the area where the subjects were during the daytime period to compare between personal and FAM ozone concentrations.

Figure 6.1, showing the relationship between the FAM and personal ozone samples for Groups 1 and 2, reveals that personal exposures were quite variable and substantially lower than fixed site concentrations. The mean personal exposures did follow the same temporal trend as the FAM data. The mean ratios of 24-hour personal to fixed site concentrations were 0.35 (Group 1) and 0.53 (Group 2). Brauer and Brook hypothesized that the differences in personal-to-fixed ambient measurement ratios were due to the relative amount of time spent outdoors: Group 1 spent less time outdoors (9%) than did Group 2 (25.8%). The personal exposures from Group 3 were quite variable. While some measurements were below the FAM concentrations, a significant number ware above it. The mean ratio of personal-to-FAM concentrations for Group 3 was 0.96, due to the fact that the participants spent the entire sampling period outdoors. An examination of duplicate personal ozone samples revealed substantial variability in measured exposures (35%). The authors concluded that the difference was due to random variability rather than true differences in personal exposure.

Liu et al., (1993) assessed ozone exposures in State College, Pennsylvania in the summer of 1991. Twenty-three children aged 10 - 11 years participated, each wearing a passive sampler for 12 hours during the daytime. Participants recorded their time-activity, which was subsequently aggregated into four groups: home, near home, school, and other. Six 12-hour indoor daytime, five 12-hour indoor night-time, four 24-hour outdoor, and one 12-hour daytime outdoor samples were collected at each home. Ambient concentrations were measured at a FAM site, along with 12-hour daytime and night-time passive samples.

Figure 6.1 Relationship Between Fixed Location (daily mean ozone concentrations) and Personal Exposure Samples for Group 1 (top) and Group 2 (bottom) Study Populations



The analysis revealed a significant correlation between the collocated passive samplers and the FAM; the Pearson's correlation coefficient was 0.95 ($p<0.01$). Twenty-four-hour outdoor concentrations measured at the FAM significantly correlated with concentrations measured outside the homes ($r=0.81$, $p<0.01$). Despite this high correlation, however, the mean concentrations at the FAM site (37.8±10.7 ppb) were significantly higher than the mean concentrations at outdoor home sites (29.8±14.3 ppb). The mean ratio of outdoor home concentrations to 24-hour FAM was 0.80±0.25. Liu et al. (1993) found differences in the ratio of outdoor to FAM 24-hour ozone levels when they grouped the homes into regions. They attributed the differences in spatial variability to population density, housing density, traffic density and the proximity of NO sources.

Twelve-hour daytime indoor concentrations exhibited a diurnal pattern, with daytime concentrations greater than nighttime concentrations (Liu et al., 1993). The results showed a significant correlation between indoor and outdoor home concentrations ($r=0.56$, $p<0.01$), suggesting that indoor levels are due to penetration of ozone indoors. The grand mean ratio of daytime indoor/outdoor (I/O) ratios was 0.45±0.23 (range 0.07-1.16). Significant differences in the mean I/O ratios by home were attributed to differences in air flow, with ratios increasing with elevated air flow.

Daytime personal exposures correlated with daytime indoor ($r=0.55$, $p<0.01$) and outdoor levels at home ($r=0.41$, $p<0.01$) and at the FAM ($r=0.36$, $p<0.01$) (Liu et al., 1993). Mean ratios of daytime personal concentrations to daytime indoor, outdoor and FAM site concentrations were 1.69 ± 3.03 (range 0.02-26.10), 0.59 ± 0.52 (range 0.01-3.44), and 0.44 ± 0.29 (range 0.01-1.35) respectively. In other words, on average personal exposures were higher than indoor concentrations, and lower than outdoor concentrations outside the home and measured at the FAM site.

A similar methodology was followed during the first phase of the Canadian Research on Exposure Assessment Modelling (CREAM) study, which measured exposures to residents in Toronto in the winter (January to March) and summer (June to August) of 1992 (Liu et al., 1995). Monitoring was conducted in 40 homes each season in the Greater Toronto Area. In the winter, indoor, outdoor and personal samples were measured weekly over three consecutive weeks; in the summer, 12-hour daytime and nighttime samples were measured for five consecutive days. Personal 12-hour daytime measurements were taken the same days. Each participant filled out a time-activity diary. Passive samplers were co-located with a FAM at a downtown site, measuring weekly ozone concentrations in the winter and 24-hour concentrations in the summer.

Tables 6.1 and 6.2 present the descriptive statistics for personal, indoor, outdoor and FAM measurements for the winter and summer (Liu et al., 1995). Wintertime personal ozone concentrations were similar to indoor concentrations, while outdoor concentrations were greater. Concentrations measured outside the home were greater during the daytime than during the nighttime. Indoor concentrations were similar for both daytime and nighttime (Table 6.2), except in the two homes with malfunctioning electrostatic air cleaners. Personal concentrations were on average similar to indoor concentrations and lower than outdoor concentrations in both seasons. The ratio of summer 12-hour daytime personal to calculated 12-hour daytime FAM concentrations averaged 0.45 (range 0-1.32).

Table 6.1 Ozone Levels During the Winter in Toronto (7 Day Average)

Sample	N	Mean	S.D.	Max	95%	90%	75%	50%	25%	Min
outdoors-home	72	15.4	6.0	31.4	23.8	23.8	18.9	13.7	11.2	0.4
indoors-home	114	1.6	4.1	29.4	4.0	2.3	1.3	0.7	0.3	0
indoors-work	38	0.7	0.7	3.1	2.8	1.4	1.0	0.5	0.2	0
personal	71	1.3	2.9	19.6	2.9	2.1	1.5	0.6	0	0
FAM	8	9.3	4.2	17.3	17.3	17.3	12.1	9.2	5.1	4.7

Table 6.2 Ozone Levels During the Summer in Toronto (12-Hour Average)

Sample	N	Mean	S.D.	Max	95%	90%	75%	50%	25%	Min
outdoors-home, day	199	19.1	10.8	54.7	42.3	33.5	24.4	19.0	11.4	0
outdoors-home, night	160	9.4	10.2	77.8	26.6	19.4	13.1	6.1	3.9	0
indoors-home, day	199	7.1	12.6	149	22.6	15.7	11.8	4.3	0	0
indoors-home, night	160	6.2	9.5	66.1	22.4	15.8	8.9	2.7	0	0
workplace, day	93	10.0	11.6	69.4	27.8	22.2	14.3	6.9	0	0
personal, day	424	8.2	8.7	52.9	25.9	19.6	11.0	6.2	2.2	0
FAM, day	12	18.4	12.6	40	40	37	28.5	16.5	9	0
FAM, 24-hour	51	15.5	9.2	47	35	26	20	14	9	1

The outdoor concentrations exhibited spatial variability between the homes and the FAM site measurements, even though the winter weekly and summer daytime measurements correlated with the FAM measurements (r=0.98 & 0.79, respectively). Concentrations were lower in the downtown area FAM sites, likely because of a higher density of NO sources and surface areas available for scavenging ozone. Liu et al. (1995) did not examine the impact of this variability on personal exposure because of insufficient time-activity information.

6.2.2 Personal Monitoring Data as Predictors of Population Exposures

Personal monitoring studies conducted in Canada and in the US have demonstrated that mean personal exposures to ozone are highly correlated with the data from FAM, suggesting that ozone data from FAM used in epidemiological studies can adequately represent population exposure.

The results of the personal monitoring studies indicate that individual exposures are quite variable, measuring lower and occasionally higher than indoor or ambient monitors. Personal exposure ranged from 0 to greater than 100% of ambient concentrations. It would be unrealistic, though, to estimate population exposures using ratios of personal to outdoor concentrations from these few studies, because the sample sizes were small and the selection of participants was not random enough to allow for generalizations to the population as a whole. However, based upon the average personal exposure measurements being less than 100% of FAM concentrations, it is reasonable to infer that population exposures will be lower than ambient concentrations, being significantly diluted by time spent indoors. Other researchers (Hayes, 1989; Weschler et al., 1992) have shown that exposure is typically dominated by ozone that has penetrated indoors from the ambient environment.

6.3 PREDICTIVE EXPOSURE ASSESSMENT

Rather than infer exposure solely from readings of ambient monitors, exposure models bridge the gap between fixed ambient monitoring data and personal exposures. The general model mathematically represents exposure as $c_m \, x \, t_m$ (NRC, 1991), where a person spends time t, in microenvironment m, having a time-averaged pollutant concentration c. Each person's exposure is computed by summing the time-weighted microenvironmental concentrations experienced by that person's visiting various microenvironments (Duan, 1982; Fugas, 1975; Sexton & Ryan 1988).

Ambient monitoring data provide the basis for estimates of ozone concentrations in different locations because ozone has no significant indoor sources (the primary source is ambient penetration). Modifiers are applied to the ambient concentration according to local influences; for example, multiplying the ambient concentration by an I/O ratio is a common approach to estimating indoor levels.

6.3.1 Microenvironmental Concentrations of Ozone

The ability to estimate ozone levels in various outdoor and indoor locations is key to characterizing individual exposure. Indoor levels of ozone are usually less than ambient concentrations. The formation, transport and destruction of ozone indoors are influenced by indoor sources (ozone generators operating to remove smells or freshen air), outside air infiltration, indoor air circulation rates, and indoor surface composition (furniture, walls, rugs, etc.). Several researchers have reported that ozone deposits onto indoor surfaces at significant rates (Reiss et al., 1994, Weschler et al., 1991).

Measurements made in various microenvironments during the summer of 1992 (Liu et al., 1995) provided mean concentrations ranging from 0 ppb (reception area) to 19 ppb (clean room). Maximum indoor concentrations ranged from 0 ppb to 72 ppb. The authors reported that the I/O ratios of ozone for both the winter (0.07±0.10) and summer (0.40±0.29) varied markedly in both seasons, with winter much lower than in summer ($p<0.05$). During summer The 12-hour daytime I/O ratio averaged 0.30±0.32 while the nighttime ratio was 0.43±0.54 (difference not significant, $p=0.45$).

The literature reports a wide range and high variability in I/O ratios (Zhang & Lioy, 1994). Indoor ozone has been measured in office buildings, museums, hospitals, residences and inside motor vehicles (McKee, 1994; Weschler et al., 1989). Most I/O ratios are in the 0.5 to 0.8 range, and I/O in residences do not appear to be different from public buildings. Weschler et al. (1989) measured simultaneous indoor and outdoor concentrations in an office-laboratory complex and reported that indoor concentrations closely track the outdoor concentrations with a diurnal pattern. However, indoor ozone concentrations measured in Houston (McCurdy, 1994) showed low and flat levels (i.e. did not display peaks). A re-evaluation of the Houston data by Johnson (cited in McCurdy, 1994) revealed statistically significant differences in indoor concentrations depending upon the use of air conditioners. Because air exchange (Ach) rates are quite low in air-conditioned buildings, how closely indoor concentrations track outdoor concentrations depends upon the tightness of the building envelope (Ach rates) and the ambient ozone levels. Indoor/outdoor ratios are high for indoor microenvironments with high Ach rates, and high ambient ozone levels; they are smaller when ambient ozone is low, due to more efficient ozone scavenging.

Liu et al. (1995) showed that wintertime I/O ratios increased significantly in homes with electrostatic air cleaners. The weekly I/O ratios averaged 0.13 ± 0.12, up from 0.07 ± 0.10. Liu et al. also showed that I/O ratios for motor vehicles are greater with the windows open (0.68 ± 0.18) than with the windows closed (0.25 ± 0.33). Johnson et al., (1995) reported median values for the vehicle I/O ratios ranging from 0.07 to 0.41, depending upon the conditions. Several of the sites monitored by Weschler et al. (1989) had office equipment that could generate ozone. At those sites, ozone concentrations indoors remained low during work hours.

6.3.2 Time-Activity Patterns

Estimates of exposure to ozone can be calculated with varying degrees of specificity, depending upon the development of exposure scenarios and the selection of values for exposure parameters (exposure frequency and duration, time-activity patterns, inhalation rate and microenvironmental ozone concentration). Commonly used default values for inhalation rate mask the inherent variability in population inhalation rates, which depend upon such factors as sex, age, weight and physical condition, as well as activity level (U.S. EPA, 1989). Standard default values for time-activity patterns are also used because of the lack of adequate activity pattern data. Population exposure estimates often do not deal with individuals who spend greater or lesser amounts of time in different microenvironments that correspond to different levels of exposure. Because ozone is primarily an outdoor contaminant, high-end exposures will occur when people are outdoors engaged in recreation or employment activities. For example, athletes and children are considered at risk to the effects of ozone because they spend time outdoors engaged in physical activity, thereby increasing both their duration of exposure and their ventilation rate. The increase in ventilation slightly increases the dose to the terminal bronchiolar region, and significantly increases the pulmonary regional total dose and the dose in the proximal alveolar region (Bates, 1994).

6.3.3 Population Exposure Estimates

Population exposure models provide an aggregate estimate of exposure for a large number of persons by combining individual exposure estimates to generate a distribution of exposures. The models simulate the movement of each person, in a specified population group, through a series of microenvironments, with each person exposed to routinely measured ambient concentrations adjusted for that microenvironment.

The probabilistic National (Ambient Air Quality Standard) Exposure Model (pNEM) provides estimates of the distribution of ozone exposures within a defined population for a specified exposure period. The exposure estimates presented here are for the general population, not a population subgroup, based upon three years of ambient air quality data. Unless otherwise specified, the results are from Johnson et al. 1994 and Zhang, 1996.

Below is a brief summary of the exposure model followed by the ozone estimates for each of the three cities. See Johnson et al. (1995) for a more detailed description of pNEM.

Overview of pNEM Methodology

The pNEM methodology consists of the following steps:

1. Define a study area, a population of interest, appropriate subdivisions of the study area, and the exposure period to be investigated.
2. Define demographic groups and microenvironments and construct a corresponding activity database.
3. Divide the population of interest into an exhaustive set of cohorts.
4. Develop an exposure event sequence for each cohort for the exposure period.
5. Estimate the pollutant concentration, ventilation rate, and physiological indicators (if applicable) associated with each exposure event.
6. Extrapolate the cohort exposures to the population of interest and to sensitive subgroups of interest.

The exposure analysis is limited to three urban areas, Montréal, Toronto and Vancouver. The areas were selected because a large percentage of the Canadian population live in and around these urban areas; each city has the minimum number of ambient monitors (three) required for pNEM. Within each city, the study area is defined as an aggregation of exposure districts. Information on the distribution of air quality data around each ambient monitor, as well as population and commuting data at the census tract level was not available. In this application of pNEM, exposure districts were constructed according to 1991 census subdivisions and linked to a FAM located in or near the subdivision. pNEM assumed that the ambient ozone concentrations throughout each exposure district could be estimated from, and represented by, data at the FAM. The number of districts for each urban area varied from seven to nine based upon the number of FAMs having valid air quality data in the study area. Monitors not considered representative of population exposure (e.g., at top of the CN Tower) were not included. The exposure period was defined as the ozone season (May 1 to September 30) within each calendar year for three years (1988-1991).

The population of interest in the exposure analysis was 5,228,455 people, 25% of the total urban population within these three cities. Each person living and working in one of the defined exposure districts was assigned to only one cohort to provide a means of linking exposure to ambient ozone levels. The model assumed that each cohort contained persons with identical exposures during the specified exposure period. Cohorts were defined by specifying home district, work district, and demographic group (defined by age, sex and working status), and residential air conditioning (AC) system. The inclusion of AC systems accounted for differences in indoor levels due to penetration of ambient ozone indoors. Identifying demographic groups according to age and working status accounted for potential differences in activity levels, which influenced the likelihood of experiencing health effects.

The cohort-specific time-activity data were provided by the Cincinnati Activity Diary study (CADS) data, collected in 1985 (Johnson, 1987). Information on both the microenvironment and the breathing rate [variable denoting slow (sleeping), slow (awake), medium or fast] associated with each activity was organized by study subject and 24-hour (midnight to midnight) time period. The diary records for one subject for a 24-hour period were designated as a 'person-day'. Each person-day is indexed by the following factors: season (summer or not summer), demographic group, temperature (cool or warm) and day type (weekday or weekend).

Justification for using the CADS database to represent the activity patterns of Canadians was provided by an analysis by Hobden (1994) which included:

- the Cincinnati study produced one of the best exposure-related time-activity databases;
- Cincinnati had a similar climatology as major Canadian cities; and
- the population of Cincinnati and surrounding area was roughly similar in size to the larger Canadian cities.

It is possible that differences in metropolitan characteristics—such as interurban distances, city lay-out and geography, route designs, public transit systems—and environmental characteristics—such as climate and latitude—all have the potential to influence how a given population uses its time. Given the uncertainties in time-activity data, and the lack of validation of many activity studies at the time of this analysis, the CADS database was the largest time-activity database available that explicitly included all of the data inputs required by the pNEM modelling methodology.

In constructing the activity data base, a computerized sampling algorithm randomly drew activity diary records relating to individual 24-hour periods from a pool of person-days which matched the cohort with respect to demographic group, and which matched the calendar day by season, day type, and temperature classification. Because CADS diary data were only available for a few days, the algorithm randomly selected data day by day from multiple subjects for the whole exposure period. This provided a better representation of the variability of exposure that was expected to occur among the persons included in each cohort.

To estimate exposures for a particular cohort, the algorithm matched the demographic characteristics of the population under study, together with the season, temperature classification and day type, with the existing categories in the activity data base for each day in the pollution season, to construct an exposure event sequence (EES). Each EES was a series of events with durations from 1 to 60 minutes at a particular combination of geographic area and microenvironment for each hour of each day for each cohort. The EES was used to determine a corresponding sequence of exposures, event-by-event.

Each exposure was defined by an ozone concentration and a ventilation rate indicator. Ozone concentration during each exposure event was assumed to be a function of the microenvironment and exposure district associated with the event. A continuous sequence of hourly average ozone concentration was developed for each combination of microenvironment and district. The microenvironment was one of:

- indoors - residence with central AC system
- indoors - residence with window AC units
- indoors - residence with no AC system
- indoors - nonresident locations
- outdoors - near road
- outdoors - other
- in vehicle

A mass-balance algorithm, described in detail in Johnson et al. (1994), generated the hourly average indoor ozone concentration during hour *h*, as a function of the indoor ozone concentrations at the end of the preceding hour (*h*-1), the ozone concentration outdoors during hour *h*, the air exchange rate during hour *h*, and an ozone decay factor. pNEM assumed that there were no indoor sources of ozone and that the concentration in a particular microenvironment was constant during a particular clock hour. Concentrations in the two ambient microenvironments (i.e. outdoors) were treated identically. This is likely to over-estimate ozone concentrations near the road because it does not account for potential ozone scavenging by nitric oxides emitted from motor vehicles.

Values for the air exchange rate and the ozone decay factor were sampled from distributions on a daily basis where appropriate (Table 6.3). Point-estimates were assumed for the parameters lacking representative databases. The opening and closing of windows in the residential microenvironments was simulated by an algorithm which specified a window status (open or closed) for each clock hour. The hourly assignments were made according to the cohorts air conditioning system (central, window units, none), the average temperature of the day, and the window status during the previous clock hour. The probabilities used in pNEM were developed from the CADS data.

Table 6.3 Exposure Parameter Values of Distributions & Point-estimates

Exposure Parameter	Microenvironment	Value
Ozone decay factor (ppb/hr)	indoors - residential and nonresidential locations	normal distribution, arith. mean=4.04; std. dev.=1.35 min=1.44; max=8.09
	in vehicle	72.0
Air exchange rate (Ach) (m^3/hr)	residence - windows closed	Lognormal distribution, geo mean = 0.53, geo. std. dev.=1.704, lower bound=0.063, upper bound = 4.47
	residence - windows open	Point estimate=6.4

	nonresidential building	Lognormal distribution, geo. mean = 1.285, geo. std. dev.=1.891, lower bound=0.19, upper bound=8.69
	vehicle	Point estimate=36

pNEM/O_3 also estimated the equivalent ventilation rate (EVR), defined as ventilation rate divided by body surface area, for each exposure event. The product of EVR and ozone concentration was defined as the dose delivered during the event. For a given age category (child or adult) and breathing rate, the algorithm simulated EVR values for each exposure event by randomly sampling from a truncated lognormal distribution. EVR values were not permitted to exceed an upper limit (EVRLIM), which varied with demographic group and event duration. The algorithm for determining EVRLIM used estimates of VO_{2max} (volume of oxygen uptake by the body), maximal and submaximal ratios of ventilation rate to oxygen uptake rate, and body surface area specific to the demographic groups associated with the cohort.

Estimates of ozone concentration, EVR, and the multiplication of ozone concentration by EVR (i.e. delivered dose) were developed for each exposure event and combined to produce time-weighted estimates for each clock hour for each cohort. The resulting year-long sequence of hourly cohort-specific estimates of exposure were extrapolated to the general population of each city by weighting according to the estimated population size of each cohort. This involves estimating the number of persons in each exposure district by demographic group, and estimating the fraction of homes falling into the three air conditioning categories. The populations of the commuting cohorts were developed from census data specific to each exposure district. In this fashion, the number of persons at risk (the sum of the estimated population size for all cohorts) was obtained for each study area.

Results of the pNEM Analyses

The following tables summarize exposure estimates for five runs of the model for the total population (including all cohorts, regardless of demographic group) within each of the three study areas for each of the three years. Multiple runs are required because pNEM is a probabilistic model. The multiple runs create a stable result based upon the empirical or theoretical probabilistic distributions of some variables. The following tables show the percentage of each study area population that was estimated to experience one or more one-hour daily maximum exposures above 82 ppb (current Canadian Ambient Air Quality Objective for 1-hour maximum ozone) (Table 6.4); the estimates for one-hour daily maximum exposures above 50 ppb (Table 6.5); the results for six-hour daily exposures above 50 ppb (Table 6.6) and the corresponding eight-hour daily exposure above 50 ppb (Table 6.7).

Table 6.4 Percentage (Standard Deviation) of the Total Study Area Population Experiencing One or More One-hour Daily Maximum Ozone Exposures Above 82 ppb.

Study Area (Population)	1988	1990	1991
Toronto (2597702)	99.39 (0.55)	82.82 (2.67)	92.05 (1.85)
Montréal (1462640)	91.86 (6.92)	30.51 (5.87)	64.44 (7.53)
Vancouver (1168113)	65.45 (2.84)	55.89 (8.01)	3.49 (2.28)

The following general statements apply to the results presented in Table 6.4. Of the nine combinations of city and year:

1. Toronto-1988 has the highest percentage of people experiencing one-hour or more, ozone exposures above 82 ppb (99.39%).
2. Vancouver-1991 has the lowest percentage of people experiencing one-hour or more, exposures above 82 ppb (3.49%) as well as the lowest percentage of people in 1988 (65.45%).
3. Montréal has the lowest percentage of people experiencing one-hour or more, exposures above 82 ppb in 1990 (30.51%).
4. Based on a three-year average for each city, the cities can be ranked from highest to lowest exposure as Toronto (91.42%), Montréal (62.27%) and Vancouver (41.61%).

Table 6.5 Percentage (Standard Deviation) of the Total Study Area Population Experiencing One Or More One-hour Daily Maximum Ozone Exposures Above 50 ppb.

Study Area (Population)	1988	1990	1991
Toronto (2,597,702)	100 (0)	100 (0)	100 (0)
Montréal (1,462,640)	100 (0)	99.24 (0.29)	99.72 (0.11)
Vancouver (1,168,113)	95.23 (1.20)	95.50 (1.23)	86.03 (2.06)

The following statements apply to the one-hour daily maximum estimates presented in Table 6.5. Of the nine combinations of city and year:

1. Toronto has the highest percentage of people experiencing one-hour daily maximum ozone exposures above 50 ppb (100%) for each of the three years. In 1988, Montréal also had 100% of the population experiencing one-hour daily maximum exposures above 50 ppb.
2. Vancouver has the lowest percentage of people experiencing one-hour daily maximum exposures above 50 ppb in each of the three years: 86.03% in 1991, 95.23% in 1988 and 95.50% in 1990.
3. Based on the three-year averages for each city, the ranking from highest to lowest exposure remains Toronto (100%), Montréal (99.65%) and Vancouver (92.25%).

Table 6.6 Percentage (Standard Deviation) of the Total Study Area Population Experiencing One Or More Six-hour Daily Maximum Ozone Exposures Above 50 ppb.

Study Area (Population)	1988	1990	1991
Toronto (2,597702)	99.97 (0.06)	98.65 (0.56)	99.74 (0.13)
Montréal (1,462,640)	97.66 (1.30)	42.05 (13.06)	98.10 (0.40)
Vancouver (1,168,113)	77.79 (0.89)	81.12 (2.92)	20.61 (6.44)

Table 6.7 Percentage (Standard deviation) of the Total Study Area Population Experiencing One or More Eight-hour Daily Maximum Ozone Exposure above 50 ppb.

Study Area (Population)	1988	1990	1991
Toronto (2,597,702)	99.63 (0.45)	94.24 (2.95)	97.49 (10.8)
Montréal (1,462,640)	95.07 (0.81)	69.00 (6.18)	95.39 (2.90)
Vancouver (1,168,113)	69.43 (2.27)	64.89 (4.18)	7.60 (4.81)

A few key features of the multi-hour exposure results of all nine combinations of city and year presented in Tables 6.6 and 6.7 follow:

1. Toronto-1988 has the highest average percentage of individuals experiencing six- and eight-hour daily maximum ozone exposures above 50 ppb (99.97% and 99.63%, respectively).
2. Vancouver-1991 has the lowest average percentage of individuals experiencing six- and eight-hour daily maximum ozone exposures above 50 ppb (20.61% and 7.60%, respectively).
3. Based on a three-year average of six- and eight-hour exposures for each city, the cities can be ranked from highest to lowest exposure as Toronto, Montréal and Vancouver.

Comparing the three-year average one-hour maximal exposures with the multi-hour exposures, as expected, more people were exposed to one-hour maximal ozone above 50 ppb than to other exposure parameters. More people were exposed to eight-hour above 50 ppb than one-hour above 82 ppb.

Limitations of the pNEM/O_3 Methodology

There is considerable uncertainty in using the modelled exposure estimates to calculate health impacts, just as there is uncertainty in extrapolating the results of pNEM to other urban areas. pNEM generates just one stochastic path as its output. Because estimates of person-days are computed from that path, estimates vary from run to run. Although McCurdy (1993) showed that an infinite number of pNEM runs are not required to produce a distribution thought to be similar to the population exposure distribution, it is desirable to be able to quantify the uncertainty in the exposure estimates. Exposures estimated from pNEM/O_3 need to be compared with those measured from a small group of individuals in demographic groups suspected to be at risk for health effects from ozone exposure.

Model distributions are dependent on the detail of information available to characterize each input parameter. Time-activity patterns are affected by land use, traffic patterns, public transit systems, recreational opportunities and environmental characteristics. Most time-activity databases have not been validated. The existing data comes from too limited an area base to make valid national estimates of population exposures. For example, outdoor workers and children are currently under-represented in the human activity data base. Exposure modelling requires a larger file of human activity patterns that better reflects the amount of time that true outdoor workers (i.e., those individuals who work outdoors at least six hours/day, on average) and children spend outside daily. Additional analysis is also required on the potential differences in time-activity between Canadians and Americans.

The season-long exposure event sequence is constructed from the data from multiple subjects and may not adequately account for the day-to day repetition of activities common to individuals.

The application of pNEM to a particular combination of city and year produces a series of cohort-specific exposure sequences. Tabulating the person-hour estimates by demographic group and time of day produces a distribution of ozone concentrations for the person-hours associated with the indicated clock hour and demographic group (i.e., a diurnal pattern of exposure). Reviewing these data indicate that exposure distributions may vary significantly from group to group when clock hour is held constant. In addition, the likelihood of exposures above a certain cutpoint can be identified by clock hour. This work has not been presented here, although it is available for the three cities.

pNEM/O_3 tends to underestimate the number of people who experience multiple occurrences of high exposure while engaged in activities. There is uncertainty around the EVR estimates used in pNEM because of the small sample sizes in the studies from which the data was obtained. Finally, there is further uncertainty in the ozone level in some indoor microenvironments because the data for air exchange rates and ozone decay rates are rather limited.

6.4 'AMBIENT' EXPOSURES COMPARED TO PREDICTED EXPOSURES

Levels of ozone measured at fixed ambient monitors (FAM) were historically, and continue to be, used as surrogates for human exposure. Ozone is measured continuously, throughout the year, at FAMs located according to land use (i.e. urban, suburban, rural and remote). Most of the Canadian population (76.6%) lives within urban areas. Urban sites exhibit two daily ozone concentration maxima, occurring mid-afternoon and during the early morning. Night-time ozone concentrations at most urban sites often attain close to 0 ppb due to ozone scavenging by NO_x emitted from cars and local industry. Urban sites experience frequent episodic, elevated concentrations of ozone, and maximum concentrations occur during the summertime (May to September).

Table 6.8 illustrates the differences in the mean ozone concentrations and frequency with which the daily maximum ambient concentrations exceed one-hour maximum of 82 ppb (current Canadian Ambient Air Quality Objective) in several areas. There is considerable year-to-year variability in the number of days with ozone concentrations above a specified concentration at individual stations. For example, in extreme years (1988) the days greater than 82 ppb are two to three times higher than the period average shown in Table 6.8.

Table 6.8 Mean Ozone Concentrations (Standard Deviation) and Average Days per Year with Ozone (1-hour) > 82 ppb (1986-1993)

Region/Site	1-hr max. ozone (ppb) (1995 and 1996)	8-hr average ozone (ppb) (1980-1992)	Average Days with Ozone >82 ppb per year (1986-1993)
Southern Atlantic	-	-	3
Montréal	35.6 (6.4), n=8	26.5 (2.4), n=6	4
Rural Québec	-	-	2
Toronto	47.3 (9.1), n=9	28.5 (1.2), n=3	15
Southern Ontario	-	-	18
Prairies	-	-	1
Vancouver-LFV	31.2 (4.1), n=12	25.8 (3.2), n=9	2

Comparing ambient ozone data with the data from pNEM (Tables 6.4-6.7) reveal that the two data sets are coherent. Toronto, that had the highest ambient ozone concentrations compared with Montreal and Vancouver, also had highest amount of predicted population exposures. A significant proportion of the total study population is exposed to daily maximum average concentrations > 82 ppb. Therefore assuming the fixed site monitoring data are representative of human exposure, more than 50% of Canadians are potentially exposed to ozone levels that cause adverse health effects, although that exposure, on average, is relatively infrequent. The pNEM data are in line with Canadian hospitalization studies (see Chapter 12.3) that have consistently shown a lower hospitalization risk associated with ozone in Vancouver and Montreal than in other parts of the country.

6.5 CONCLUSIONS

Exposure assessment involves estimating the intensity, frequency, and duration of human contact with ozone. Ozone levels vary from year to year depending on the meterological conditions; hot, sunny summers usually produce higher ozone levels than do cool, rainy summers. Individual and population-estimated exposure also varies from year to year. Exposure is defined as any contact at a boundary between a person and a specific ozone concentration for a specified time interval.

Direct personal monitoring studies measure the concentration of ozone in the immediate microenvironment (breathing zone) of the person. Results from these studies indicate that personal exposures follow a similar temporal pattern to that from FAM monitoring. This supports that FAM data are representative of population exposure. Personal exposures can be higher but are usually lower than FAM data. Generally, outdoor measurements overestimate personal exposures by greater than 50%. The studies have reported wide variability in individual personal exposures, and have demonstrated that the amount of time people spend in a given location significantly influences exposure. This second point is supported by other human exposure field studies (conducted over the years) indicating that time-activity patterns are the most important determinant of a person's exposure (Ott, 1989).

The personal monitoring data were collected over relatively long averaging times. Because ozone builds and declines gradually over the course of the day in urban and non-urban areas, varying degrees of individual exposure are associated with the hourly concentrations. The 12-

hour, 24-hour, and weekly averaging exposures collected using the passive sampler cannot assess hourly exposures, even though shorter times (such as 1-hour maximum) are considered more relevant for the health effects. Short-term ozone concentrations within a community vary much more rapidly in time and space than do long-term average concentrations. Personal monitoring data have not been very useful in predicting population exposures due to small sample sizes and unrandom selection of participants in those studies.

Monitoring the concentration of ozone in various microenvironments, integrating the data with the time spent in each, and summing the time-weighted microenvironmental concentrations over a specified time period produce an indirect estimate of exposure. Simple models have been developed (Brauer & Brook, 1995; Johnson et al., 1995; Liu et al., 1993; Liu et al., 1995) and validated using the personal monitoring data, to indirectly predict personal exposure. The models are poor predictors of personal exposure when only one outdoor and only one indoor microenvironment are factored into the model. The predictive ability of the models improves as more microenvironments are considered. The poor predictability of many models using ambient data is likely due to the poor relationship between outdoor and indoor ozone levels. Indoor ozone levels generally follow the diurnal pattern of ambient levels only in 'leaky' buildings. Most indoor microenvironments are 'tight', and indoor ozone levels remain low and quite flat.

Given the wide spatial and temporal variability in both ozone concentrations and time-activity, probabilistic models estimate exposure by combining all the principle elements of the source-to-receptor pathway. Specifically, pNEM uses detailed information on human activity patterns, indoor-outdoor ratios, and air exchange rates to predict how many days a "typical person" in a subpopulation cohort will be exposed above any given level during a specified exposure period. Outputs of the exposure model can be used to directly estimate population exposure by multiplying the outcome for the typical individual by the size of his or her cohort. The data are presented as frequency distributions for the general population, which include everyone who resides in the geogrqphic region being modelled.

By incorporating additional information about time-activity patterns, ventilation rates, and demographics into the exposure assessment, thus increasing the complexity of the input, exposure modelling indicates that a large percentage of the total population is exposed to ozone at concentrations greater than 82 ppb (the current Canadian Air Quality Objective). As would be expected, the predicted absolute number of person-days of exposure to the one-hour daily maximum and 8-hour average ozone is higher in regions with higher ambient ozone levels. Of the three cities modelled, person-days of exposure are greatest for Toronto residents, moderate for Montreal residents, and lowest for Vancouver residents.

Extrapolating the modelled results to the Canadian population leads to a prediction of greater person-days of exposure in southwestern Ontario, followed by southern Ontario, Montréal, the Southern Atlantic Region, and the Lower Fraser Valley. Exposure varies from year to year depending on time-activity patterns. During hot, sunny summers, time spent outdoors is greater, thereby increasing the likelihood of peak exposures. Not everyone, however, comes in contact with ozone levels measured at the FAMs. Therefore, when ambient data from FAMs are used to predict exposure, the total population living in the area has the potential to be exposed, but population exposure is usually overestimated.

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7 EFFECTS ON MATERIALS

Since the NO_x/VOC Assessment Program did not address the issue of ozone effects on materials, an independent review of the literature was undertaken. This review of ozone effects on materials is current to the end of 1996.

Although sulphur dioxide remains the most important pollutant in the degradation of materials, other atmospheric pollutants are gaining in importance as a result of declining emissions of sulphur dioxide. Ozone is one of these. As with other photochemical oxidants, ozone damages many types of materials both functionally and aesthetically. Ozone is sufficiently chemically active that even at low ambient concentrations the effect of material exposure to ozone can be observed (North Atlantic Treaty Organization (NATO), 1974). In the last ten years or so, it has become more apparent that that due to the high reactivity and complex chemistry of ozone, the effects of ozone on all materials can only be properly understood if one considers its interactions with other pollutants (ICP, 1996; Tidblad and Kucera, 1996; UN ECE, 1995). In addition, other atmospheric parameters such as temperature, sunlight and humidity can influence the impact of ozone on materials. Although the importance of these synergistic effects is noted, a full review of these effects is not appropriate for the purposes of this Science Assessment Document.

This chapter reviews the effect of ozone on elastomeric materials, textiles, dyes and pigments, surface coatings (paint) and metals and other building materials. Most of the research on the effects of ozone has been done on organic materials. Significant portions of this chapter are based on reviews by the United States Environmental Protection Agency (U.S. EPA,1996), the North Atlantic Treaty Organization (NATO,1974) and Lee, Holland and Falla, (1996) in the United Kingdom.

7.1 ELASTOMERIC MATERIALS

One of the earliest techniques used to assess ambient ozone was based on the consistent and rapid cracking of stressed rubber strips when exposed to ambient air. Either the time until cracking or the depth of cracking after a specified time could be related to ambient ozone concentrations (U.S. Dept. of HEW, 1970; Vega and Seymour, 1961). That cracking of rubber can be used effectively as an indicator of ozone concentrations has also been recently confirmed (Serano et al., 1993).

Elastomeric materials are long chain unsaturated organic molecules. Exposure of ozone to an elastomer results in a breakage of the molecular chain at carbon-carbon double bonds. One plausible effect mechanism is that ozone attacks elastomers by adding a chain of three oxygen atoms directly across the double bond, forming a five-membered ring structure. This structure rearranges to form a zwitterion and an aldehyde. The aldehyde-zwitterion pair can be formed on either side of the chain scission. Subsequent reactions of the zwitterion lead to a permanently oxidized elastomer (U.S. EPA, 1996). This mechanism of chain scissioning explains why saturated polymers such as silicones, ethylene, butyl rubber, and propylene are inherently resistant to ozone damage. In contrast, the effects of ozone on natural rubber, general purpose diene rubber, and synthetic polymers of polyisoprene, polybutadiene, acrylonile-butadiene and styrene-butadiene, can be extremely damaging due to their high content of main chain unsaturated carbons (Lee et al., 1996.). Polymers such as polyethylene, polypropylene, nylon, and polystyrene appear to be embrittled by high ozone concentrations (ozone concentration>1000 ppm), but at current ambient ozone levels, effects are not significant (Lee et al., 1996). Neoprene, on the other hand, is highly unsaturated, but is highly resistant to crack growth due to the electronegative chlorine atom adjacent to the double bond (Lee et al., 1996).

In an unstressed state, the chain scissioning only occurs to a shallow depth of 0.5 μm and appears as a white bloom or a surface frost (Lee et al., 1996). The reaction rate of ozone at the polymer surface is several orders of magnitude faster than in the bulk material. The rate constants at 20° C have been determined for several polymers and range from 1.2×10^{-2} L/mol·s for polyisobutylene, to 4.4×10^{5} L/mol·s for polyisoprene (Razumovski & Zaikov, 1983). Sub-surface elastomeric material can be accessed by ozone during the formation of surface cracks. Surface cracks, during contortion, will expose a fresh elastomeric inner surface which can subsequently be attacked by ozone. In a non-stressed state, sub-surface polymers are not susceptible to ozone, even when they are exposed to ozone for a long duration (NAT0, 1974). An exposure period of 16 hours to 1500 ppm ozone caused no observable effect in non-stressed natural and synthetic rubbers (Tucker, 1958).

Elastomers are usually used in varying degrees of stressed states. Tensile stresses of 2-3% are enough to make the elastomer vulnerable to ozone concentrations of 0.01 - 0.02 ppm. Cracks will appear perpendicular to the direction of the applied stress (Lee et al., 1996). As cracks deepen, elastomers mechanically weaken. It is also believed that some of the adhesive properties of certain rubbers are reduced (Lee et al., 1996).

Degradation of elastomers also occurs as a result of exposure to other pollutants and to natural weathering processes; in particular, to sunlight. The importance of these factors, relative to the effect of ozone, is an ongoing area of research (Lacoste et al., 1994; Tidblad and Kucera, 1996). Unfortunately, the damaging effects of sunlight can be difficult to distinguish from those induced by exposure to ozone (Yocum and McCaldin, 1968; Yocum and Upham, 1977).

Methods, such as the utilization of wax and antiozonant coatings, have been developed to protect elastomers from ozone degradation. Amorphous or microcrystalline and paraffinic waxes form a non reactive barrier between the ozone and the elastomer (Jowette, 1983). Wax coatings can be used more effectively in conjunction with antiozonants. An antiozonant forms a protective barrier in which the substance protects the elastomer, by itself reacting with the ozone. The most effective antiozonants are all N,N' derivatives of p-phenylenediamine (Lattimer et al., 1984).

There are currently two primary theories as to how antiozonants chemically protect polymers (Lattimer et al., 1984). 'The scavenger theory', suggests that antioxidant additives diffuse across the surface of the polymer, where they form a protective layer and react with the ozone sacrificially before the ozone scissions the double bond of the material (U.S. EPA, 1996). 'The protective film theory', also assumes a diffusion of the antiozonant to the surface of the polymers, but the protective layer is less reactive with ozone than the double bond, therefore sealing the double bond away from the ozone (U.S. EPA, 1996).

In addition to these two primary theories, other theories have been proposed. 'Relinking theory', predicts that the antiozonants are involved with the repair of the scissioned double bond (Lattimer et al., 1984). 'Self healing film theory', predicts that the antiozonant reacts with the daughter molecules formed from the ozonolysis, creating a low molecular weight inert film that prevents ozone from further penetration (Lattimer et al.,1984). It is likely that more than one protection mechanism is in operation in each situation (Lattimer et al., 1984).

Protective layers (the wax, antiozonant or laminant) are also subject to degradation. Antiozonants must diffuse to the surface of the elastomer to be effective, but in doing so they become vulnerable to external damage during normal usage such as abrasion. Oil, gasoline, and other chemical agents such as acidic deposition (Lee et al., 1996) may leach them (NATO, 1974). Removal of the antiozonant reduces ozone protection, therefore effectively decreasing the functional lifetime of the product.

Chemical protection of polymers from ozone can be improved via hydrogenation (the removal of the double bond with a substitution of a hydrogen atom) or the use of saturated polymers in the elastomers composition. The hydrogenation process is a complex time consuming process due to the material's viscosity and the high molecular mass (Lee et al., 1996). The substitution of all unsaturated polymer materials for saturated ones to increase the resistance to ozone is not always viable. Substitutions may change the desired physical properties of the elastomer, such as resilience and resistance to stress relaxation. Applications for saturated polymer products are limited and presently they account for less than 10 percent of elastomer consumption (Lee et al., 1996).

Antiozonants appear to aid in the long term protection of elastomers, but once a first crack is formed, oxidation is likely to continue until component failure. Higher ambient temperatures increase diffusion of the antiozonant to the polymer surface (U.S. EPA, 1993), thus increased temperature aids the ozone protection of the elastomer. Fortunately, ambient ozone concentrations correlate well with high temperatures, when the antiozonant is most effective (U.S. EPA, 1996).

Table 7.1 lists the available concentration response studies. The lowest ozone concentration at which effects were observed on elastomeric materials is 0.02 ppm (20 ppb). At this level, cracks were observed in stressed vulcanized rubber strips after relatively short periods of time (Bradley and Haagen-Smit, 1951).

7.2 TEXTILES

Cellulose fibers (such as cotton or silk) can be affected by ozone via the same mechanisms as elastomers (unsaturated double bond cleavage). The degradation caused by ozone results in a reduction of the tensile strength and other physical properties. Degradation is indirectly assessed by measuring changes in textile fluidity (NATO, 1974).

Sunlight, heat, alternate wetting and drying, and micro-organisms are factors that also contribute to the weathering and deterioration of textiles. The effect of textile exposure to these factors (for example, when clothes are outside exposed to ambient air) is greater than the deterioration of fiber caused by ambient ozone (NATO, 1974). In general, the contribution of ozone to the degradation of fabrics has not been well quantified, but is considered insignificant (U.S. EPA, 1996). However, Bogaty et al. (1952) and others have demonstrated the synergistic effects of moisture and ozone on fabrics. Low levels of ozone can degrade fabrics if they are sufficiently moist.

Table 7.2 lists the available concentration response studies. The lowest ozone concentration at which effects are observed is 0.02 ppm (20 ppb) (Bogarty et al., 1952). At this level, the tensile strength and fluidity of duck and print cotton cloth is demonstrably reduced. However, these effects only occurred when the cloth was wet. Dry cloths exposed to 0.02 ppm ozone did not show any significant effects.

Table 7.1 Ozone effects on elastomers and polymers (adapted from U.S. EPA, 1996)

Material	Concentration	Exposure Time/Conditions	Effect	Comment	Reference
polyethylene polystyrene polypropylene nylon	1000ppm	-20 hour exposure in the presence of UV radiation -control was run under ambient ozone conditions of 20 ppb	-embrittlement	-it would take the control 114 years to achieve the same degree of embrittlement	Lee et al., 1996
automotive tires	0.25-0.5 ppm (ozone) 0.04 ppm (ambient air)	LABORATORY STUDY -no exposure time specified -tires were mechanically stressed FIELD STUDY -greater than 1 year exposure -actual service use	-cracking of white side wall	-there was a positive correlation between the laboratory test and the field test	Hofmann and Miller, 1969
vulcanized rubber strips	0.02-0.46 ppm and 20, 000 ppm (ozone)	-3 to 65 min exposure -material was mechanically stressed (100% strain by bending)	-surface cracking appeared in 1 sec. at high concs. and in 5 mins - > 1 hr. at low concs.	-dose–response curves were developed	Bradley and Haagen-Smit, 1951
rubber tires and various polymers	0.023 to 0.048 ppm (ambient air)	-150 to 700 hours exposure -physical stress -this was a field study (ambient air)	-time of cracking was observed	-cracking occurred over a broad range of values and was related to the stress	Meyer and Sommer, 1957
SBR: Plysar S and Plysar Krylene	0.25 ppm (ozone)	-19 to 51 hours exposure -temperature was 120° C -100% strain -test was conducted with and without antiozonants	percent of antiozonant was related to the cracking depth	-dose–response curve was developed on unprotected rubber	Edwards and Storey, 1959
polyisoprene	0 - 1.8 ppm (ozone)	-2 hour exposure -temperature was 22° C	-cracking and stress relaxation	-rates of attack were proportional to ozone concentration	Razumovskii et al.,1988 Cont.

Table 7.1 cont. Ozone effects on elastomers and polymers (adapted from U.S. EPA, 1996)

Material	Concentration	Exposure Time/Conditions	Effect	Comment	Reference
white side wall specimens	0.05 to 0.5 ppm (ozone)	-250 - 1000 hrs exposure -10 and 20% strain	-cracking rates were determined for varying stress and ozone concs.	-2 - 5 years of ambient air required for ozone cracks to penetrate cord depth	Haynie and al. 1976
10 different NR, SBR, and CR formulations	0.5 ppm (ozone)	-up to 300 hours exposure -temperature was 30° C -were tested with and without antiozonant protection	-time to 10% to 20% relaxation	-both formulation and protection affect relaxation	Ganslandt and Svensson (1980)
natural rubber, epoxidised rubber and co polymer	0.05 to 1000 ppm (ozone)	-16 hour exposure -20 to 70° C -10 to 100% strain	-time to first cracking	-temperature dependence of the antiozonants was observed	Lake and Mente (1992)
several NR/SBR blends, with and without protection	0.05 to 0.15 ppm	-3 to 16 hour exposure -sunlight -humidity	-interply adhesion affected at 0.05 ppm and above	-both antiozonants and waxes are needed for protection against sunlight plus ozone	Davies (1979)
tire cords (nylon 66; Dacron polyester; Kevlar aramid)	0 to 1.5 ppm (ozone)	-0 to 48 hour exposure -UV light -heat (100°C) -rh (20 to 90%) -NO_2	-RFL adhesion loss occurred primarily during 6 hour exposure to high rh and 0.2 ppm ozone	-synergism between ozone and rh -RFL deterioration occurred at the surface	Werghoefer (1974)

Table 7.2 Ozone effects on textiles (adapted from U.S. EPA, 1996 and NATO, 1974)

Material	Concentration	Exposure Time/Conditions	Effect	Comment	Reference
duck and print cotton cloth	0.02 ppm and 0.06 ppm	-50 days exposure -experiment conducted in absence of light -wet (≥50% moisture content) and dry cloths were exposed to ozone; wet cloths were also exposed to clean air	-reduction in fluidity and a 20% loss in tensile strength in ozone exposed wet samples -control cloths retained much of their tensile strength and fluidity	-ozone at low concentration can oxidize cellulose -ozone level more effectively degrade fibers if they are kept sufficiently moist (ozone is more soluble in water than air at room temperature)	Bogaty et al., 1952
print cotton cloth	0.5 ppm	-50 days exposure -absence of light -21°C, 72% rh	-no effect on fluidity or breaking strength	moisture content of cloth (9%) too low to produce degradation when exposed to ozone	Morris (1966)
print cotton cloth	0.75 ppm	-60 days exposure -absence of light -25°C -every 3 days half the samples were machine washed, the other half were soaked in water for 1 minute -control sample was not exposed to ozone -excess water was removed from all samples via a wringer system	-control sample showed no significant change in tensile strength -ozone exposed samples showed an 18% and a 9% loss in tensile strength for the machine and water soaked samples respectively	-the increased degradation of machine washed samples may have been due to the alkalinity of the detergent	Kerr et al., 1969 Cont.

Table 7.2 cont. Ozone effects on textiles (adapted from U.S. EPA, 1996 and NATO, 1974)

Material	**Concentration**	**Exposure Time/Conditions**	**Effect**	**Comment**	**Reference**
modacrylic, acrylic, nylon 66, polyester	0.2 ppm	-7 days exposure -artificial sunlight -~39% rh -48° C -cloth wetting for 18 minutes every 2 hours -control was not exposed to ozone	-slight reduction in breaking of acrylic and nylon fibers as compared to the control -no change was observed for the modacrylic and polyester fibers	-synthetic fibers not as affected by ozone as the cellulose fibers	Zeronian et al., 1971
nylon yarn	0.03 ppm	-up to 445 days exposure -dye yarn with acid blue 45 and acid blue 122	-fibers lost ability to be dyed	-exposure to ozone affected the dye ability of the fiber	Makansi, 1986

7.3 DYES AND PIGMENTS

7.3.1 Textile Dyes

In the early 1900s, oxides of nitrogen were considered the major active fading agents. It was not until 'o-fading' (the bleached appearance of faded fabrics exposed to ambient air in areas of low NO_x) was observed, that a search for another oxidant capable of colour fading began (Salvin & Walker, 1955). The products most affected were cotton and polyester garments and nylon carpets. Ozone was identified as being the causal agent in the fading (NATO, 1974).

Many textile dyes react with ozone, causing the colour of the dye to fade. The colour change is the result of ozone molecules breaking the aromatic ring portion of the dye molecule, oxidizing the dye. The daughter molecules that result from this oxidation process can be differently coloured than the parent or colourless. Consequently, the original dye colours become altered or faded (U.S. EPA, 1996). With certain dyes, the effect of direct sunlight cannot be distinguished from that of ozone (Yocum and McCaldin, 1968; Yocum and Upham, 1977). As with impacts on the textiles themselves (section 7.2), ozone exposure alone fails to produce a large amount of colour fading. High moisture levels or relative humidity are also required. For example, when nylon carpet was subjected to ozone, humidity levels of at least 65% rh were required to produce pronounced colour fading. Generally, fading decreases rapidly below 65 % rh (NATO, 1974).

The chemical nature of the textile fiber and the dye can be used to predict the degree of ozone fading that is likely to occur. The chemical structure of the dye and the fiber determine the degree to which fiber and the dye remain associated. Ability of the dye to dissociate from the fiber, diffuse and migrate along the surface plane of the textile is directly related to the fading observed (Haylock & Rush, 1976).

Two important fiber characteristics in ozone-induced fading are the cross-section modification ratio and fiber draw ratio (orientation of the polymer chains) (Haylock & Rush, 1976). An increase in the modification ratio will increase the cross-sectional area and subsequently increase ozone penetration and fading. Increases in the draw ratio, however, will increase the number of fibers oriented in the same direction as the fiber polymer chains which decreases the amount of ozone-caused fading (Haylock & Rush, 1976).

Other factors that influence the dye degradation are: the manner in which the dye is applied, the presence of protective agents, ambient temperature, relative humidity, the presence of other air pollutants, and the amount of strain the textile fiber undergoes due to folding, creasing, and stretching and the chemical nature of the dye itself. Higher molecular weight dyes will diffuse more slowly than lower molecular weight dyes and subsequently, are less susceptible to ozone induced fading.

Certain combinations of dye type and textile type may increase immunity to ozone fading. Some dyes are inherently immune to ozone fading independent of the substrate textile. Studies have shown that ozone has no fading capabilities on royal blue acetate, red rayon-acetate, or plum cotton dyes (U.S. EPA, 1996). However, some combinations of textile and dye increase the fiber's susceptibility to ozone. Low ozone levels (0.02 - 0.05 ppm) are able to fade sensitive fibers such as red and blue dyes in cellulose acetate, viscose and cotton muslin (U.S. EPA 1996).

The available database on the effect of ozone on fabric dyes does not permit the derivation of meaningful dose-response relationships. Much of the literature is qualitative in nature, with little detail given as to ozone exposure concentrations. Comparisons among studies are difficult given that temperature and humidity conditions vary from one study to another and relative humidity is known to be an important factor in ozone induced fading. Nonetheless, there is clearly good evidence that exposure to ozone does induce fading (U.S. EPA, 1996).

Table 7.3 lists the available concentration response studies. The lowest ozone concentration at which textile dye impacts have been observed is 0.02 ppm (20 ppb) (Ajax et al., 1967). However, the concentrations in the Ajax et al. (1967) experiment are questionable (U.S. EPA, 1996). A more reliable LOAEL for effects of ozone on textile dyes is therefore 0.05 ppm (50 ppb). At this level, a large variety of dye - fabric combinations are prone to fading.

7.3.2 Artists Dyes

Ozone causes the degradation, particularly fading, of artists' pigments in paintings and other important cultural assets. In addition, where these pigments are applied to organic materials (e.g. paper), these too may be susceptible to the effects of exposure to ozone. Due to the uniqueness of works of art, these ozone-induced changes are considered unacceptable (U.S. EPA, 1996). Generally, artist dyes are part of cultural items, e.g., artworks, and are not typically exposed to ambient conditions, being protected in indoor environments. However, indoor environments are not devoid of ozone.

Given that art and museum collections are intended to be preserved for great lengths of time, most recommendations for the protection of such materials are for concentrations of ozone in the indoor air to be limited to 1 ppb ozone (Cass et al., 1991). The implications of this for the protection of outdoor art are significant, given that ambient ozone levels are generally far higher than this. Outdoor ozone concentrations can also be a major determinant of indoor ozone concentrations (see Chapter 6), depending on the building's ventilation system. Works of art that are subjected to high air ventilation rates in museums (2 or 3 air changes per hour) will encounter a higher dose of ozone and will subsequently experience greater degradation (U.S. EPA, 1996). Druzik et al. (1990) have found that in museums, art galleries and historical houses, the indoor / outdoor ozone ratio ranged from 0.10 to 0.87. Some fading has occurred in current collections, but it is not possible to distinguish light-induced fading from chemically-induced fading (Cass et al., 1991). The use of display cases (that are removed from normal air circulation) and framing behind glass provide some protection against fading. The use of ozone resistant pigment and coatings are encouraged to reduce the susceptibility (Cass et al., 1991).

The concentrations of ozone used to induce fading in controlled dose-response studies are higher than those that usually exist in ambient museum air, yet the results are arguably applicable to the issue of protecting art over the longer term (Cass et al.,1991). There is evidence from controlled exposure studies that the fading of artists' pigments in the presence of ozone is directly related to the product of exposure concentration x exposure duration. If true, then an art collection exposed to 0.001 ppm (1 ppb) of ozone for 100 years will be affected similarly (in terms of fading) as one exposed to 0.4 ppm (400 ppb) of ozone for 90 days (Cass et al., 1991). The latter exposure (400 ppb over 90 days) has been shown to produce severe fading of many artists' pigments (Shaver et al., 1983; Whitmore and Cass, 1988). This model is therefore potentially useful for evaluating the long-term effects of ozone, without long term experimentation.

Table 7.4 lists the available concentration response studies for artist pigments and dyes. The lowest concentration at which effects were observed in response to ozone exposure alone is 0.4 ppm. (This was also the lowest experimental concentration tested in these studies). At this level colour fading occurs in traditional organic colourants, Japanese colourants and various artist colourants in 95 days, according to a number of studies. Cass et al. (1991) found effects on alizarin crimson (on watercolour paper) in 7 days at an exposure of 0.4 ppm ozone.

Table 7.3 Ozone effects on textile dyes (adapted from U.S. EPA, 1996)

Dye	Textile	Concentration	Exposure Time/Conditions	Effect	Comment	Reference
blue & red	drapery	0.1 ppm	-no exposure conditions specified -dyes were tested with and without antiozonant	-dyes without antiozonant were markedly bleached while samples that contained antiozonant were not	-oxidants caused dye fading, not NO_x	Salvin and Walker, 1955
disperse	cellulose acetate	laboratory exposure to auto exhaust (approx. ozone conc. of 0.02 - 0.55 ppm field exposures not reported	-54 hours exposure -69 dye-fabric combinations -SO_2 was present in the reaction vessel -tests were conducted in rural and urban areas using light-proof cabinets 3 months exposure period	-photochemical by-products of irradiated auto exhaust caused more fading than non-irradiated samples or SO2 and clean air combination - a more than additive effect was observed for $SO_2 + O_3$ (lab. and field exposures)	-reported laboratory concentrations are questionable -temperature and humidity were not the primary cause of dye fading but were principal contributing fading factors (field exposures)	Ajax et al., 1967
direct, fiber reactive vat, sulphur, azo	cotton					
disperse	polyester					
disperse, basic	orlon					
disperse, acid	nylon taffeta					
direct	viscose					
premetolized, acid	wool					
direct red 1	cotton	0.05 and 0.5 ppm	-12 weeks exposure -temperature is 55° F and 90° F -50% and 90% rh	-both the 0.05 and 0.5 ppm ozone levels induced fading	-increased temperature and humidity increased the amount of fading, but ozone's effect appeared to be more dependent on high rh	Beloin, 1973
direct red 1	rayon					
acid red 151	wool					
reactive red 2	cotton					
basic red 14	acrylic					
azoic[b] red	cotton					
acid orange 45	nylon					
acid yellow 65	wool					
basic yellow 11	acrylic					
sulphur green 2	cotton					
acid violet 1	wool					
direct blue 86	cotton					
disperse blue 3	cellulose acetate					cont.

Table 7.3 Ozone effects on textile dyes (adapted from U.S. EPA, 1996)

Dye	Textile	Concentration	Exposure Time/Conditions	Effect	Comment	Reference
disperse blue 3	nylon					
disperse blue 27	cellulose acetate					Cont.
disperse blue 27	polyester					
reactive blue 1	cotton					
reactive blue 2	cotton					
vat blue 14	cotton					
AATCC O_3 ribbon	acetate					
olive I and II disperse blue 3 and 7	nylon	0.2 and 0.9 ppm	-1 to 6 hours exposure -70% to 90% -40° C temperature	-linear fading dependent on [ozone], increased rh increases the amount of fading	-increased fiber characteristics such as draw ratio reduced fading -increases in fiber characteristics such as modification ratio increased fading -increased temperature increased the fading observed -increased fiber surface area increased fading	Haylock and Rush, 1976
disperse blue dye in an avocado green mixture	nylon 6 yarn	0.05 ppm	-time duration not specified -85% rh -temperature was 40° C	-fading related with fiber surface area, namely the diameter		Hueval et al., 1978
2 disperse dyes, 2 acid dyes	nylon 6 and nylon 66 carpet	not specified	-3 months to 3 year time duration -experiment was conducted on 28 homes around the country	-geographic and seasonal variation was notice in the fading	-a field study experiment	Nipe,1981 Cont.

Table 7.3 Ozone effects on textile dyes (adapted from U.S. EPA, 1996)

Dye	Textile	Concentration	Exposure Time/Conditions	Effect	Comment	Reference
disperse blue 3	nylon 6 yarn	0.2 ppm	-time duration was 2 to 120 hours -65%, 85%, 90% rh -temperature was 40° C	-time caused a nearly linear increase in fading -fading rate was largely dependent on rh		Kamath et al., 1983
disperse, basic disperse direct vat, sulphur, fiber reactive disperse disperse, acid direct acid, mordant	acrylic cellulose acetate cotton polyester nylon viscose rayon wool	not specified	-time duration was for 2 years -time interval was every 3 month -experiment was conducted in light proof cabinets	-2/3 of the sample experienced significant ozone fading	-this was a field study at rural and urban sites	Beloin, 1972
disperse blue 3 Acid blue 25 Acid blue 40 Acid blue 45 Acid blue 80 Acid blue 127	nylon 6 and 66 yarn	0.2 ppm	-time duration 0 to 96 hours -85% rh -40° C	-fading proceeded consistent with diffusion of dye to fiber surface	-changes of the dye's morphology towards the production of a more compact fiber to reduce dye mobility and ozone fading -use of high molecular weight dies will slow down diffusion	Moore et al., 1984
royal blue red plum plum	drapery rayon acetate rayon acetate cotton duck	0.5 and 1.0ppm	-time duration 250 to 1000 hours -50% and 90% rh -NO_2 and SO_2 were added to the reaction vessel	-statistically relevant ozone fading did not occur	-this was a laboratory study -no synergistic relationships could be determined among pollutants	Haynie et al., 1976

Table 7.4 Ozone effects on artist dyes (adapted from U.S. EPA, 1996)

Material	Substrate	Concentration	Exposure Time/Conditions	Effect	Reference
17 watercolour pigments	paper	0.4 ppm	-time duration 95 days -temperature 23° C -47% rh	-only alizarin-based watercolours were very sensitive -all other pigments showed less fading	Shaver et al., 1983
alizarin, alizarin crimson, anthaquinone	silica gel, cellulose Teflon	0.4 ppm 0.4 ppm 10 ppm	-time duration 95 days -temperature 22° C -50% rh -time duration 18 - 80 hours -temperature 24° C -≤40% rh	-each pigment tested faded on all substrates	Grosjean et al., 1987
16 traditional organic colourants	paper	0.4 ppm	-time duration 12 weeks -temperature 23° C -50% rh	-11 colourants reacted while 3 possibly reacted of the 16	Whitmore et al., 1987
indigo, dibromoindigo, thioindigo, tetrachlorothioindigo	Teflon	10 ppm	-time duration 4 days	-all faded, but indigo and dibromindigo were consumed	Grosjean et al., 1988a
currcumin	cellulose, watercolour paper, silica gel, Teflon	0.4 ppm 0.4 ppm 0.4 ppm 10 ppm	-time duration 95 days -temperature 25° C -50% rh -time duration 4 days -temperature 24° C -≤20% rh	-all faded to colourless endpoints -water colour paper was slower to react	Grosjean et al., 1988b
traditional Japanese colourants and dyes	paper silk cloth	0.4 ppm	-time duration 12 weeks -temperature 22° C -50% rh	-several organic and one inorganic dye faded significantly	Whitmore and Cass, 1988 Cont.

Table 7.4 cont. Ozone effects on artist dyes (adapted from U.S. EPA, 1996)

Material	Substrate	Concentration	Exposure Time/Conditions	Effect	Reference
triphenylmethane colourants	Teflon	10 ppm	-time duration 4 days - temperature 24° C -$\leq$20% rh	-colourants with unsaturated carbons may fade	Grosjean et al., 1989
Alizarin crimson	watercolour paper	0.4 ppm	7 days 22°C and 50% RH dark	severe fading of unframed sample framed sample behind glass exhibited virtually no fading	Cass et al., 1991
various artists colourants	watercolour paper cellulose	mixture of: 0.02 ppm ozone 0.01 ppm PAN 0.08 ppm NO_2	-time duration 12 weeks -temperature 16 to 24° C -46 to 83 % rh -35 colourants were tested	9 colourants experienced substantial change, 11 colourants experienced negligible change, 12 colourants, small change and 3 colourants, modest change	Grosjean et al., 1993

7.4. SURFACE COATINGS (PAINT)

A surface coating is a material (paint, varnish or lacquer) which is applied to a substrate. It forms a coherent film for the intent of decoration or protection of substrates such as wood, metal, stone, plastic and composite substrates (Lee et al., 1996). A paint is a finely powdered pigment, dispersed in polymeric binder material which functionally holds the pigment to the surface (U.S. EPA, 1996).

Ozone has the ability to affect both the binder and the pigment in the paint, causing premature aging (ICP, 1996). The mechanism of deterioration is via the oxidation of the organic binder material similar to the mechanism of elastomeric degradation. The resulting damage is manifest as erosion (gradual weathering) of the paint, as well as cracking, peeling, and discolouration (NATO, 1974; U.S. EPA, 1996). Of these effects, erosion of the paint surface is the most studied with respect to air pollution effects. Discolouration arises from the oxidation of the pigment to daughter products which have a noticeably different colour or are colourless (U.S. EPA, 1996). The degree to which ozone will affect the paint varies by the type of paint, temperature, duration of wetness, wind speed, sunlight (Haynie & Spence, 1984), moisture and the concentration of other pollutants such as sulphur dioxide and nitrogen oxides (U.S. EPA, 1996). It is likely that the combination of these other factors will have a larger impact on the paint degradation than the degradation caused by ozone alone (Table 7.5).

Erosion of painted surfaces can be measured as a loss of weight, then converted to a loss of thickness of the paint coating; this approach has been used in some studies. However, there are recognized limitations to this approach, and it is evident that changes in weight of the surface coating may not arise solely from erosion of the binder and pigment in the coating (Lee et al., 1996). A number of damage functions for ozone-induced paint erosion have been reported in the literature, but the results are questionable (U.S. EPA, 1996). Haynie et al. (1976) exposed oil-based house paint, latex house paint, vinyl coating and acrylic coil coating to 0.5 and 0.05 ppm concentrations of SO_2, NO_2, and O_3, in different combinations. Significant ozone-induced damage to acrylic and vinyl coil coatings was observed, although the erosion rates were very slow. Analysis of the effect of ozone concentration on acrylic coil coating yielded a linear regression of

$$\text{Erosion rate} = 0.159 + 0.000714\,[O_3]$$

The calculated erosion rate is presented in micrometers per year, and $[O_3]$ is the concentration in micrograms per cubic meter (Haynie et al., 1976). Paint erosion from exposure to high ozone concentrations is predicted to be substantial by this linear relationship. However, at ambient ozone concentrations, erosion of paint is predicted to be insignificant. This linear regression predicts that a 20-μm thick coating would last over 80 years exposed to an average ozone concentration of 0.05 ppm (U.S. EPA, 1996).

Campbell et al. (1974) also studied the effects of ozone in combination with sulphur dioxide, on panels painted with different surface coatings (automotive refinish, latex coating, coil coating, industrial maintenance coating, and oil-based house paint). The panels were expose to low (0.1 ppm) and high (1.0 ppm) concentrations of ozone and sulphur dioxide over periods of approximately 0, 200, 350 and 500 days (Table 7.5). Significant increases in erosion rates were observed at high pollutant concentrations, with oil based house paints experiencing the largest increase (compared to control panels). The most ozone resistant coating was the automotive finish. However, ambient (0.1 ppm) concentrations of ozone did not produce statistically significant increases in erosion rates of any of the surface coatings (U.S. EPA, 1996) (Table 7.5).

Spence et al. (1975), (reviewed by Lee et al., 1996), also investigated the effects of combined exposures to ozone, sulphur dioxide, nitrogen dioxide and relative humidity on a number of paints. Both high and low exposures, and different exposure durations, were included in the study protocol. Although Lee et al. (1996) expressed some concern over the methodology used to measure erosion, the study was cited as providing evidence that high ozone concentrations (33 times urban background levels of approximately 15 ppb) are capable of eroding durable industrial coatings after about 40 days exposure.

Lee et al. (1996), extrapolating from the dose-response relationships of Campbell et al. (1974) and Spence et al. (1975), and assuming a linear dose-response relationship, were able to predict that in general, an increase in atmospheric ozone concentrations of 15 ppb, would result in an increase in the rate of erosion of between 1 and 2%, depending on the nature of the coating. The validity of this result was strengthened by the fact that the analysis of both the Campbell et al. (1974) and Spence et al. (1975) studies, which used different methodologies, yielded comparable results. The authors point out though that erosion is not the sole mechanism for degradation of surface coatings. Embrittlement, cracking, loss of adhesion, loss of gloss and soiling are all factors that should be taken into account (Lee et al., 1996).

Table 7.5 lists the available concentration response studies. The lowest ozone concentration that is supported by the concentration response data is 0.05 ppm (50 ppb). At this ozone concentration, there is a slow, observable erosion of coil coating (Haynie et al., 1976).

Table 7.5 Ozone effects on surface coatings (adapted from U.S. EPA, 1996)

Material	Concentration	Exposure Time/Conditions	Effect	Comment	Reference
latex and oil house paint, vinyl coil coating and acrylic coil coating	0.05 and 0.5 ppm (combinations of O_3, NO_2 and SO_2)	-250, 500 and 1000 hour durations -50 and 90% rh -13 ad 35° C and artificial dew and sunlight cycles	-statistically significant ozone-caused damage on acrylic and coil coatings -very slow erosion rates of coil coating	-chamber experiment conducted with SO_2 and NO_2	Haynie et al. 1976
automotive refinish, latex, coil coating, industrial maintenance coating, oil house paint	0.1 and 1.0 ppm (O_3 and SO_2)	-up to 1000 hour duration -substrate was stainless steel panels -70% rh -temperature was 65° C -artificial dew and sunlight cycles	-1ppm ozone significantly deteriorated the finish -0.1ppm ozone did not significantly deteriorate the finish	-chamber experiment conducted with SO_2	Campbell et al., 1974
automotive refinish, latex, coil coating, industrial maintenance coating, oil house paint	ambient exposure; no pollutant measurements	-up to 24 month duration -substrate was stainless steel panels	-erosion was greater in polluted, urban areas	-field conditions for: • clean rural site • moderately polluted site • high SO_2 site • high NO_2 site	Campbell et al., 1974
oil-base house paint, acrylic latex house paint, vinyl coil coating, acrylic coil coating	0.08 ppm and 0.50 ppm O_3, in combination with high and low levels of NO_2 and SO_2	250, 500 and 1000 hour durations - 35° C - artificial dew and sunlight cycles - high (90%) and low (50%) RH	- oil-base house paint had the highest erosion rate - vinyl and acrylic coil experienced low erosion - latex house paint erosion rates were invalid due to reaction with SO_2	- chamber experiment - 16 different combinations of SO_2, NO_2, O_3 and RH at two levels	Spence et al., 1975
latex and oil house paint	0.006-0.055 ppm	-3 to 30 month time duration -substrate was stainless steel	-effects of ozone were not independently statistically significant	-field conditions at 9 sites in St. Louis	Mansfeld, 1980

7.5 METALS AND BUILDING MATERIALS

In contrast to its effect on organic materials (see previous sections), ozone on its own has little ability to affect inorganic materials (e.g. metals and building materials). However, the presence of ozone in a sulphur dioxide-containing environment accelerates the corrosion of zinc, silver, aluminum, nickel, iron, and copper, among other metals (Graedel et al., 1984; Druzik, 1985; Svenson and Johannson, 1993; ICP, 1996).

The work of Svenson and Johannson (1993) has shown that in the presence of ozone, the uptake of sulphur dioxide by zinc was greatly increased. In turn, this increased the amount of sulphate formed at the surface of the metal, thereby enhancing the corrosion process. The corrosion of zinc in the presence of ozone alone was negligible. The results indicated the ozone reacts with the loosely bound four valent sulphur on the surface of the zinc. The formation of the sulphate ion creates an electrolytic solution that has a corrosive effect on the protective surface oxide layer of the metal, exposing the underlying metal to corrosion. (The zinc corrosion layer, however, has much less zinc oxide (if any) than, for example, does a steel surface layer have iron oxides, given that zinc oxide produces zinc carbonate in the presence of atmospheric CO_2.) Although this study was limited to zinc, there is no reason to suppose that ozone accelerated, sulphur dioxide induced corrosion is restricted to zinc (Lee et al., 1996). Other metals may well be similarly affected.

Another interesting aspect of the work of Svenson and Johannson (1993) is that they were able to demonstrate that the acceleration of sulphur dioxide oxidation and deposition on zinc by ozone becomes greater as the sulphur dioxide concentration decreases. That is, as sulphur dioxide concentration decreases, the effect of ozone becomes increasingly important. This is significant given that, as authors Lee et al. (1996) have emphasized, sulphur dioxide and ozone concentrations are often out of sync, with sulphur dioxide peaking in wintertime, and ozone in the summer.

Ozone's effect on metals is influenced by environmental factors (e.g. temperature, humidity/wetness) in addition to the chemical composition of the atmosphere. Concentration-response relationships have been defined for steel, zinc, aluminum, copper, and bronze, for weight loss (WL in g/m^2) as result of studies conducted over a 4 year ozone exposure period. These clearly reveal the importance of the combined effects of both chemical and environmental factors (UN ECE, 1995):

- For weathering steel: WL = 85 + 0.26 TOW $[SO_2][O_3]$ + 432 TOW
- For zinc: WL = 14.5 + 0.043TOW $[SO_2][O_3]$ + 80 Rain $[H^+]$
- For aluminum: WL = 0.85 + 0.0028 TOW $[SO_2][O_3]$
- For copper: WL = 19.3+ 0.011 $[SO_2][O_3]$ + 162 Rain $[H^+]$
- For bronze: WL = 11.8 + 0.047 TOW $[SO_2][O_3]$

  Where $[SO_2]$ is the sulphur dioxide concentration ($\mu g/m_3$), $[O_3]$ is the ozone concentration ($\mu g/m_3$). Rain is the amount of precipitation in m/yr, $[H^+]$ is the concentration, TOW is time of wetness or when rh>80% and temperature is greater than 0°C (represented as a time fraction of the duration of the exposure).

Stone is also subject to degradation outdoors as a result of exposure to both natural weathering and anthropogenic pollutants. Both SO_2 and NO_x are known to cause the deterioration of calcareous stone (ICP, 1996; Haneef et al., 1992). In the case of SO_2, the critical reactions are thought to involve an attack on either Ca (OH_2) or $CaCO_3$ by sulphuric acid, leading to the formation of gypsum, which can crystallize within the pores of the building material (ICP, 1996, Haneef et al., 1992). The oxidation of SO_2 to sulphuric acid involves water and the presence of atmospheric oxidants such as ozone. The degradation of building material by NO_x has received comparably less attention. The key reactions involve the oxidation of NO_x in the presence of water to form calcium nitrate (ICP, 1996; Haneef et al., 1992). The calcium nitrate formed is quite soluble, however, and may be quickly washed off the surface of the stone.

Marble, a natural stone, is widely used as a building material. The presence of ambient pollutants can accelerate the surface erosion of marble (Haynie et al., 1976) and lead to diminished aesthetic value. A concentration-response relationship has been developed from experimental studies to predict the erosion occurring on the surface of a marble structure:

$$E = -3.31 + 0.078\,rh + 2.95 \times 10^{-3}\,[SO_2] + 3.33 \times 10^{-3}\,[O_3]$$

where E is the erosion rate in ($\mu m/yr$), rh is the relative humidity (%), $[SO_2]$ is the sulphur dioxide concentration ($\mu g/m_3$) and $[O_3]$ is the ozone concentration ($\mu g/m_3$) (Haynie et al., 1976).

Again, clearly ozone is not acting alone, but in combination with other factors. Erosion rates predicted by this regression are quite low. If we accept that the results of an exposure over several weeks can be extrapolated to several centuries, then the erosion that is predicted from exposure to 0.03 ppm of ozone, and 0.03 ppm sulphur dioxide, over 300 years, is 1 mm of marble.

Haneef et al. (1992) used an atmospheric flow chamber to investigate and quantify the effects of SO_2, NO_2 and NO on a number of stone materials, both wet and dry. These pollutants were added as single exposures or in combination with ozone, to further understanding on the role of ozone as an oxidant in the chemical reactions occurring on building materials. Pollutant concentrations within the experimental chamber were 10 ppm, which allowed realistic presentation rates of the pollutants to be used. A 30-day exposure period and four different stone types were used (Table 7.6).

Dry stones showed little weight gain in the presence of SO_2, NO_2 and NO. In the presence of ozone, however, all stones showed a weight increase and often these were considerably greater than that which occurred in the absence of ozone (e.g. 6x greater than for NO and NO_2 alone on Portland limestone). All wet stones showed large weight increases after exposure to SO_2 and small weight losses after exposure to NO and NO_2 alone. Similar results occurred when O_3 was added to the experimental treatment. Weight changes of the wetted stones reflected the net result of chemical reactions and leaching of reaction products. Analysis of water-soluble anions revealed the presence of sulphates and nitrates, the amount of which was dramatically increased in the presence of O_3. The study was designed to investigate the mechanism of stone degradation and in particular the role of ozone in this degradation, but did not utilize a range of exposure concentrations that would allow formulation of concentration-response relationships.

Table 7.6 lists the available concentration response studies. The lowest ozone concentration at which effects can be observed cannot be identified due to the complex nature of ozone's synergistic relationship with SO_2 and NO_x. Experimentation involving a variety of co-exposures (varying each pollutant concentration independently) would aid the determination of an effect level.

Table 7.6 Ozone effects on metals and building materials

Material	Concentration of Synergistic Components	Exposure Time/Conditions	Effect	Comment	Reference
zinc surface covering galvanized steel	18 ppb SO_2 50 ppb O_3 50 ppb NO_2	-all 3 gases were tested separately and in various combinations -70% and 95% rh	-zinc was corroded far most effectively in combinations of NO_2 and SO_2, and O_3 and SO_2 than each gas separately -NO_2 and SO_2 combination was less corrosive than SO_2 and O_3 combination	-there is the suggestion of a synergistic relationship	Svennson and Johansson, 1993
copper	-various concentrations and combinations of NO_2, SO_2, and O_3	-humidified -25° C -another trial was run at a higher humidity of 75 rh	-reaction of O_3 alone with the copper produced CuO and $Cu(OH)_2$ which manifest as a decrease in the surface content of mono-valent copper	-synergistic effects of SO_2, and O_3 were more pronounced at a higher humidity - O_3 more effectively oxidizes SO_2 (to sulphate) than NO_2	Zakipour et al. (1995) (cited in Ortech, 1996)
White Cherokee marble	0.49 ppm and 0.098 ppm	-exposure time1000 hours -90% rh -temperature was 35° C -chamber study -synergistic effects of SO_2 and NO_x were studied	x-ray microprobe line scans revealed that sulphur penetrated the sample abut 50 µm -weight loss analysis showed erosion of up to 21.8 µm/yr	-ozone, in a high SO_2 atmosphere can erode marble	Haynie et al., 1976 Cont

Table 7.6 cont. Ozone effects on metals and building materials

Material	Concentration of Synergistic Components	Exposure Time/Conditions	Effect	Comment	Reference
Pentelic marble Mansfield sandstone Massangis limestone Portland limestone	10 ppmv of SO_2, NO_2 and NO, alone or in combination with 10 ppmv of O_3	-time duration 30 days -84% rh -chamber study -both wet and dry trials were run	-the influence of ozone increased the degradation of the stone in all cases -wetted stones with pollutant gases and ozone gave the following order of reactions: $SO_2+O_3>NO_2+O_3>NO+O_3$ -the largest degradation occurred with wetted Portland limestone with SO_2 and O_3 which yielded a loss of 67.1 mg of calcium equivalents	-ozone reacts synergistically with other pollutants -wetting aids the synergistic effect soluble anions extracted from stones and run-off revealed the presence of sulphates and nitrates	Haneef et al., 1992

7.6 RESEARCH NEEDS

There is little question that ozone is affecting a variety of materials, alone and as a result of synergistic effects with other pollutants. There are clear causal mechanisms to account for the interaction of ozone at the molecular level with organic materials, and for the synergistic impacts of ozone and other pollutants on inorganic materials. For regulatory purposes, what is needed is a better characterization of concentration-response relationships. To date, there have only been a few investigations that have provided this type of information. Clearly this task is complicated by the synergistic nature of the reactions of ozone with other pollutants and environmental variables. Field studies, at ambient pollutant concentrations are required but clearly evaluation of such studies is complicated by the presence of multiple pollutants in the ambient air.

Useful information might nevertheless be obtained by choosing carefully exposure sites where climatic and pollution data are well known and where the concentrations of pollutants vary (Tidblatt and Kucera, 1996). If in addition, the experimental protocol involves exposing a range of materials that are known to react differently to the synergistic effects of different pollutants, the possibility of separating the effects of different pollutants (especially NO_x and O_3 since concentrations of these pollutants are usually highly correlated), is enhanced. Such a program is currently underway as a 4 year exposure progam under the UN ECE (1997-2001), based on the results of the previous 8 year UN ECE program (1987-1995). The new program includes a Canadian exposure site at the Dorser Research Center.

It is also very difficult to assess the existing database on the effects of ozone on materials because of differences in the methodologies employed in different studies, and differences in and difficulties with reporting the observed effects quantitatively (e.g. quantifying the degree of fading and cracking vs. a simple observation that fading or cracking appeared). Some standardization of procedures for investigating and quantifying the effects of ozone on different materials is required.

7.7 SUMMARY

Review of the literature indicates that ozone damages many different types of materials functionally and aesthetically. The damage is caused at the molecular level by chain scissioning and cross-linking mechanisms. In some cases there is an added synergistic degradation of materials due to the presence of other ambient pollutants, specifically sulphur dioxide and nitrogen oxides.

Among the stretched elastomer materials tested, natural rubber, general diene rubber, polyisoprene, polybutadiene, acrylonile-butadiene and styrene-butadiene were most affected by ozone. Neoprene, silicones, ethylene, butyl rubber and propylene were not observably affected by ozone. Protection of elastomers can be increased by the use of antiozonants and waxes.

Ozone has the ability to damage textiles by reducing tensile and break through strength. Among the textiles tested, cellulose fibers, such as cotton or silk, suffer the greatest tensile strength reduction when exposed to ozone, while synthetic fibers, such as acrylic, modacrylic, nylon and polyester, are not noticeably affected. Factors such as sunlight, heat, moisture and microorganisms can also cause reduction in tensile strength.

Ozone has the ability to fade or discolour dyes. Lower molecular weight anthraquinone dyes appear to fade most quickly while dyes such as royal blue (rayon-acetate), red (rayon acetate) and plum (cotton) were not observed to fade. A number of artist pigments were found to fade in the presence of ozone. Fine art dyes, such as in cultural exhibits, can be protected by limiting exposure to ozone or through the use of ozone resistant pigments or coatings.

Ozone has the ability to erode surface coatings by reacting with the binder and/or the pigment. High concentrations of ozone do cause paint erosion, although low (ambient) concentrations have little effect. Oil based house paints were most susceptible to ozone damage while automotive finishes and paints were the most ozone resistant. Other factors that contribute to paint erosion are temperature, moisture, sunlight, and the presence of other ambient air pollutants. These factors are considered to be of greater importance than ozone in affecting the erosion rates of paints and other surface coatings.

The impact of ozone on metal and building materials is primarily a result of synergistic effects with sulphur dioxide. The corrosion of metals, such as zinc, silver, aluminum, nickel, copper and iron is accelerated in the presence of both ozone and sulphur dioxide. Ozone alone appears to have little effect on metal corrosion. Stones materials, such as marbles, sandstone, limestones, bricks, concrete, and gravel, are also affected by synergy between ozone and sulphur dioxide.

Studies conducted in ambient air are prone to the variability of that environment. The variability in the concentrations of synergistic ambient variables could make interpretation of data increasingly difficult due to the complexity of synergistic relationships. Attempts were made in some laboratory studies to mimic the ambient environment, via the inclusion of some other variables (e.g., humidity, high temperature and UV penetration). At times, modelling was used to approximate damage that would occur in the ambient environment.

For the majority of materials examined, effects were reported qualitatively (e.g., fading/cracking). Even though concentration response relationships were identified for paints, metals and marbles, the way in which the effects of ozone were quantified was diverse (each relationship predicted either a quantified erosion rate, cracking, or weight-loss). Also, inconsistencies in mathematical expression of the relationship (e.g., linear, and synergistic) hampered the merging of the results into an overall concentration response relationship for materials.

The effect levels demonstrated for the different material types are listed in Table 7.7. It should be noted that these effect levels were by and large obtained under very specific laboratory conditions and are not necessarily representative of real world conditions. No effect level was determined for metals and building materials due to the complex nature of synergistic relationships with sulphur dioxide and nitrogen oxides.

Table 7.7 Lowest Observed Adverse Effect Level (LOAEL) for Ozone Effects on Materials		
Material	**Lowest Observed Adverse Effect Level**	**Experimental Conditions**
elastomers	0.020 ppm (20 ppb)	5 mins., mechanically stressed
textiles	0.020 ppm (20 ppb)	50 days, wet cloths
textile dyes	0.050 ppm (50 ppb)	12 wks., 50% and 90% RH, 55° F and 90° F
artist dyes	0.4 ppm (400 ppb)	7 days, dark, 22 and 50 % RH
surface coatings	0.05 ppm (50 ppb)	250, 500 and 1000 hrs., O_3 in combination with SO_2, NO_2, 50 and 90% RH
metals and building materials	not determined	not applicable

Ozone impacts on elastomers and textiles were observed at levels as low as 0.020 ppm (20 ppb), while the lowest concentration at which impacts on textile dyes and surface coatings were observed was 0.050 ppm (50 ppb). Although the lowest observed concentration at which effects were noted on artists' dyes was .4 ppm (400 ppb), this concentration induced severe fading of the artists' dye. Further, Cass et al. (1991) have proposed that evidence exists for effects on artists' dyes to be a function simply of exposure concentration x exposure duration. Given the long periods of time over which artists' works require preservation, it is likely that effects would be observed at much lower concentrations if sufficiently long exposure durations were considered.

Recognizing the variability of confounding contributions of other atmospheric parameters (light, temperature, relative humidity and other air pollutants), it is not possible to define a single lowest observed effect level for the effect of ozone on materials. The data suggest that the level above which ozone effects are demonstrated on materials is in the range of 20-50 ppb, and that the effects observed at this level may be exacerbated by the presence of other atmospheric parameters.

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NATIONAL AMBIENT AIR QUALITY OBJECTIVES FOR GROUND-LEVEL OZONE

SCIENCE ASSESSMENT DOCUMENT

A Report by
the Federal-Provincial Working Group
on Air Quality Objectives
and Guidelines

July, 1999

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Part 4 of 7

Canada

8 EFFECTS ON VEGETATION

The information presented in this chapter has been extracted from the Report of the Vegetation Objective Working Group of the NO_x/ VOC Science Assessment (Multistakeholder NO_x/VOC Science Program, 1997, VOWG). The mandate of this group was to review the current state of knowledge on ozone damage to Canadian vegetation, and to develop a position on the appropriate form and level of an ambient ozone air quality objective to protect vegetation. Given this mandate, and the VOWG's understanding of the revised framework for setting ambient air quality objectives in Canada (see Preface), which involves first, identification of Reference Levels, the VOWG report focussed on providing the information that would form the scientific basis for setting a Reference Level for ozone effects on vegetation. Subsequent to the VOWG review, the literature was reviewed to end of 1997 and relevant material included in this assessment.

8.1 QUALITATIVE TOXICITY ASSESSMENT

Photochemical oxidant air pollution was first recognized in 1944 when Middleton et al. (1950) observed toxic effects on vegetation in Los Angeles. These symptoms most closely resembled those caused by peroxyacetyl nitrate (PAN) or by mixtures of PAN, aldehydes and other highly oxidizing chemicals. Later, Richards et al. (1958) ascribed grape 'stipple' near San Bernardino, California, to atmospheric ozone. Tobacco 'weather fleck' observed at Beltsville, Maryland, in 1952 and in southern Ontario in 1955 was attributed to ozone in 1959 (Heggestad & Middleton, 1959; MacDowall et al., 1963). Etiological studies to determine the relationship between atmospheric ozone and unexplained needle injuries on Eastern white pines were started in Canada in 1959 (Linzon, 1966) and in the U.S. in 1961 (Berry & Ripperton, 1963).

Although ozone injury was first observed and documented under field conditions in the Los Angeles area, the majority of research that followed through the 1950s to the 1970s was conducted with pot-grown plants under greenhouse or controlled environment conditions. The advantages of this approach were good reproducibility under specific pollutant exposure and climatic regimes, exhaustive evaluation of exposure-response functions, and, in some cases, detailed examination of the physiological, biochemical and morphological effects of the pollutant on the receptor. However, as research efforts gradually began to focus on the biological relevance of the early findings, more effort was directed towards field exposure studies, and a search for meaningful exposure functions that would enable policy setters to predict the impact of season-long ozone exposure on agricultural and forestry industries.

Plant response to ozone is based on a sequence of biochemical and physiological events that can result in foliar pathologies (visible injury), altered carbohydrate allocation leading to reduced growth and yield, as well as impacts on the competitive relationships within plant communities and ecosystems (Guderian et al., 1985). These types of effects are summarized below.

8.1.1 Biochemical, Metabolic and Physiological Effects

The effects of ozone on the biochemical, metabolic and physiological processes of plants have been extensively reviewed and discussed in recent publications (Runeckles & Chevone, 1992; Guderian, 1985; Legge & Krupa, 1986; Unsworth & Ormrod, 1982; and Darral, 1989). Accordingly, these documents have been used in the development of the overview summary that follows. Unless otherwise or specifically cited, the source of the following material should be ascribed to all of these excellent review publications.

Ozone can affect a fairly wide array of cellular processes once it has entered the leaf via open stomata. Once inside, the dividing line between biochemical and physiological effects is difficult to differentiate since the resulting physiological effects have their origins in the chemical reactions of ozone with cellular constituents. Under certain conditions, resistance or detoxification mechanisms can alter the entry of ozone into the plant leaf or result in its initial detoxification once inside the intercellular air spaces and mesophyll cell walls (i.e., the apoplastic space outside the plasmalemma). Once inside the symplast, ozone that has not been detoxified in the apoplast acts first at the biochemical level to impair the functioning of various cellular processes.

The current understanding of resistance or detoxification mechanisms is still in a state of relative uncertainty. Under certain conditions, physiological responses to ozone exposure may protect the plant by excluding ozone from the leaf interior. Specifically, exposure to very high levels of ozone can result in reductions in rates of stomatal conductance. The mechanism is not well understood, but it has been shown in one study to be related to histological changes in guard cells and resultant loss of stomatal control. This response is often labeled as an exclusion or resistance mechanism. Reductions in stomatal conductance in plants exposed to lower concentrations of ozone have been attributed to increased internal leaf CO_2 concentrations, resulting from ozone-induced reductions in biochemical CO_2 fixation; however, more research is needed in this area, as some evidence also exists that under certain conditions, ozone can cause stomatal opening.

Some degree of oxidation and cleavage of waxes at the leaf surface can occur and this can lead to changes in composition and physical properties of the leaf surface (e.g., decreased water repellence); it would also result in reduced ozone levels available to enter plant leaves. Once inside the intercellular air spaces and mesophyll, ozone is thought to persist mainly as O_3, although superoxide anion and hydroxyl radicals are also formed. These oxidant species are reactive with cellular components, such as ascorbate, olefins such as ethylene, terpenoids, hydroxyl ions, as well as major cell-wall constituents such as cellulose, lignin and pectins. Because these oxidant species are additionally produced in the cell as a result of photosynthetic processes, and are injurious to cell constituents, plant cells have evolved enzymatic mechanisms to transform these oxidative species to less toxic constituents. Ascorbate, peroxidase, glutathione reductase and superoxide dismutase, to name the most commonly cited (Runeckles & Chevone, in Lefohn, 1992), are assumed to have some role in detoxifying oxidant species resulting from ozone exposure, as well as those resulting from normal cellular activity.

There are conflicting studies regarding the role of superoxide dismutase in the reduction of products from ozone interactions with the cytoplasm; there are also reports of increased peroxidase activity and decreased diamine oxidase activity that could reduce the impact of ozone by increasing the scavenging of potentially harmful hydrogen peroxide and by increasing di- and polyamine levels. In any event, these " detoxification" enzymes are saturable, and as they are oxidized themselves in the process of reducing oxidative species, require cycling back to the reduced state before being available for further detoxification 'work'. The reduction of these enzymes requires a reductant (NADPH, reduced ferredoxin, etc.), a number of which are formed by energy requiring processes in the mitochondria.

These exclusion or detoxification mechanisms certainly reduce the amount of ozone which can react with photosynthetic and respiratory components. The role of exclusion and detoxification mechanisms in differential ozone sensitivity among species or cultivars is not well understood, in that there does not appear to be a unifying model of how resistance is acquired by a plant. It seems clear that detoxification of ozone or its products would burden the cells' energy budget, although whether this additional burden would decrease productivity, relative to direct effects of ozone on photosynthesis for example, is not known.

In their review, Runeckles and Chevone (1992) have further subdivided the biochemical effects into the following functional areas:

Chloroplast metabolism

- effects on sulfhydryl groups and enzymes of the reductive pentose cycle;
- direct reaction of ozone with ascorbate, resulting in its removal as a peroxidase substrate and the potential generation of hydrogen peroxide;
- effects on chloroplast ATP levels and an influence on the dark reactions of the Calvin cycle in the stroma;
- decreased Hill reaction activity;
- indirect effects on Photosystems I and II;
- possible effects on nitrogen metabolism;
- chlorophyll destruction; and
- effects on the integrity of the envelope and thylakoid membranes that perturb the chemi-osmotic status and the balance of proton and other ionic flows.

Photorespiration and Respiration

- changes in the mitochondrial structure can affect the respiration process; and

- photorespiration, involving reactions within the chloroplast, the cytoplasmic glyoxysomes and the mitochondria, can be affected by alterations in the oxygenase function of rubisco (with impacts on CO2 release).

Carbohydrate Metabolism

- effects on enzymes related to carboxylase and oxygenase functions within the rubisco process can lead to effects on carbohydrate translocation and the carbon and energy economies of the plant.

Nitrogen Metabolism

- effects on nitrate reductase activity within the chloroplast and on glycine and serine within the photorespiratory pathway;
- changes in nodulation of the roots of legumes related to the supply of photosynthate from the shoots; and
- possible ozone scavenging due to effects on polyamine generation via diamine oxidase inactivation.

Organic Acids and Lipids

- possible changes in lipid and fatty acid fractions resulting from direct chemical reactions with ozone (lipid decomposition and formation of malondialdehyde) or indirectly via alterations in respiration, photorespiration and amino acid metabolism.

Secondary Metabolism

- although very little direct evidence has been published, the role of ozone in the generation of phenolics, flavonoids, alkaloids, terpenoids, betalains and glucosinolates, which are linked with foliar pigmentation and senescence processes appears to be important.

The major physiological processes affected by these alterations are reductions in photosynthesis and increased leaf senescence. The effects on photosynthesis include impacts on stomatal conductance, photosynthetic capacity, carbohydrate allocation and respiration. The photosynthetic capacity of a plant plays a major role in plant response to stresses in the environment and is also associated with foliar nitrogen content and with water movement, both of which are, in turn, related to carbohydrate allocation. As a result, reductions in photosynthetic capacity have the potential to adversely affect growth patterns, leaf repair and overall growth and reproductive capacity. One of the major impacts of altered carbohydrate allocation is on the availability of carbohydrate resources to the roots and associated mycorrhizal fungi, as the plant tries to meet the needs of foliar repair or redirects carbohydrates towards increased leaf production to compensate for foliar loss resulting from ozone stress. Ozone induced changes in canopy density, root/shoot ratios and stem growth also can affect the functioning of the plant and render it more susceptible to other stresses.

In their summary of the effects of ozone on cellular permeability and leakage, Runeckles and Chevone (1992) provide an overview of the linkages that must be taken into consideration in the overall evaluation of ozone impacts on plant growth:

> *Although changes induced by ozone may involve specific chemical reactions that exert direct effects on metabolic processes, it is important to recognize that many effects may be mediated by changes in membrane structure and function that profoundly influence the physiology of the affected cells, the tissues in which they occur, and, hence, the plant as a whole. Plant responses that result in visual changes in foliar characteristics are secondary processes of ozone toxicity, which appear after initial defense mechanisms are overrun. Cellular biochemical and physiological alterations occur without such visible injury symptoms appearing, and these modifications affect critical metabolic functions capable of limiting oxidative stress and ozone toxicity both directly and via more complex physiological interactions within the cell. It is the integrated cellular system that confers and determines plant sensitivity to ozone.*

8.1.2 Acute and Chronic Foliar Injuries

As with many other pollutants, ozone effects on plant foliage can be categorized into acute and chronic effects. Acute symptoms on broad-leaved plants consist of chlorosis, fleck, stipple and uni- or bifacial necrosis. On conifers, acute responses consist of mottle, banding and chlorosis (Krupa & Manning, 1988). Plants have the capacity to compensate for acute effects, depending on the respite time between acute exposures and on plant phenology when the initial stress occurred (Lefohn & Runeckles, 1987).

Chronic symptoms are related to frequent, relatively low hourly ozone concentrations, with periodic, intermittent peaks of relatively high hourly concentrations. Chronic effects can lead to changes in plant growth, productivity and quality, and these effects may occur without visible symptoms. When symptoms do develop, they can include chlorosis, delayed early season growth, premature senescence and leaf abscission (Manning & Krupa, 1992). In the case of acute effects, plants can compensate for stress during respite periods; therefore, the frequency of ozone episodes and the time interval between such episodes are critical in evaluating and modelling plant response (Krupa & Kickert, 1989; Lefohn & Runeckles, 1987).

It is well established that foliage is the primary site of plant response to ozone exposure. It is also known that ozone exerts a phytotoxic effect only if a sufficient amount reaches sensitive sites within the leaf. Thus, ozone injury will not occur if the rate of uptake is low enough that the plant can detoxify the ozone or is able to repair or compensate for the effects (Tingey & Taylor, 1982). Effects at the cellular level are ultimately expressed as visible injury to the leaf or as secondary effects that can be expressed as reduced root growth, reduced yield of fruits or seeds, or both. The main factor in the ultimate impact of ozone exposure on growth or yield of individual plants involves a determination of whether ozone directly or indirectly impacts a metabolic or physiological process that is or may become a limiting factor in plant growth at the time of exposure.

Exhaustive lists of plant foliar sensitivity/resistance to ozone under short-term, controlled-environment conditions have been published (Guderian et al., 1985; Heck et al., 1977). However, there is uncertainty surrounding the relationship between plant foliar injury and life cycle yield and biomass alteration resulting from season-long ozone exposure under field conditions.

There is still interest in some of the earlier exposure-response information on foliar injury, as this may assist decision - makers in the development of short-term protection for crops or other types of plants where injury can affect marketability or aesthetic values. Comprehensive reviews of the available literature were made by Jacobson (1977) and Linzon et al. (1975), and concentration-time profiles for short exposure, acute foliar injury were developed for sensitive, intermediate and resistant species. This three-tier classification system is of limited use in terms of its direct application to current crop species and cultivars. Much of the information came from genetic lines and plant species that were chosen for study due to their sensitivity to ozone; the classification system is quite old; and most of these lines and cultivars are no longer in commercial use. However, the classification system does provide benchmark information that should be considered in any effort to develop ozone air quality objectives.

Based on these and other findings, Guderian et al. (1985) developed a set of maximum acceptable ozone concentrations, which, if met, would provide reasonable protection of vegetation from short term, acute exposures. These thresholds are shown in Table 8.1.

Table 8.1 Exposure thresholds for plant response (foliar injury) to ozone (from Guderian et al., 1985).

Duration of exposure (hours)	Ozone concentration by category of plant resistance (ppb)		
	Sensitive	Intermediate	Resistant
0.5	150	250	500
1.0	75	180	250
2.0	60	130	200
4.0	50	100	180

8.1.3 Growth, Yield and Productivity Impacts

Crops

The importance of short-term, controlled-environment ozone exposures and associated thresholds for foliar response has been overshadowed in the last 10-15 years by the shift in research priorities to natural, ambient exposure assessments under full season, field grown conditions. The main reason for this shift was the growing body of evidence that indicated foliar injury was not an acceptable surrogate for ozone impacts on crop yield or tree growth. In many studies, significant reductions in yield or biomass growth were being detected in the absence of foliar symptom development, while in other cases, plants were able to sustain considerable foliar injury with no detectable loss in yield or productivity (U.S. EPA, 1995).

With the trend away from foliar injury assessment, the concept of 'damage' has developed (Guderian et al., 1985) as a measure of impairment in the intended use of the plant. This includes reductions in aesthetic values, the occurrence of foliar injury, and loss of weight, number, or size of the plant part intended for harvest. Loss in yield may also include changes in physical appearance, chemical composition, or the ability to retain quality features during storage. Loss of aesthetic value includes negative impacts on the appearance and marketability of ornamental plants or crops in which the foliage is paramount.

Any assessment of yield or quality parameters under field conditions is complicated by the ubiquity of ozone exposure, the effect of meteorological variables on ozone distribution within crop canopies, and the effect of numerous biotic and abiotic factors which can alter plant response. Some of these difficulties have been partially overcome by refinements made in the field assessment techniques, including open-top chambers, open air fumigation systems, and ambient air pollutant gradients (Ormrod et al., 1988). To date, however, no one research technique has solved all of the problems associated with research on this regional-scale, ubiquitous pollutant.

A comprehensive program designed to address the issue of season-long ozone impact on agricultural crop yield was the National Crop Loss Assessment Network (NCLAN) in the U.S. This seven-year program (1980-86) was initiated by the Environmental Protection Agency in 1980 and consisted of experimental exposures of 38 different crop species/cultivars at five geographic sites, chosen to represent distinctly different climatic conditions in regions growing different crop species. Open-top chambers were used to expose different agricultural crops to various regimes of ozone and sulphur dioxide. Plant yields were measured to determine exposure-response relationships and to assess the national economic consequences resulting from the exposure of major agricultural crops to ozone. The results of this program are described in numerous publications (Heck et al., 1982, 1983, 1984a, 1984b).

In the U.S. EPA criteria document on ozone impacts (1986), the review of all NCLAN and related yield response studies resulted in the following main conclusions:

- current ambient levels of ozone in many parts of the U.S. are sufficiently elevated to impair the growth and yield of plants;
- the NCLAN study and supporting field studies using chemical protectants show that effects on plants occur with only a few hourly ozone concentrations above 0.08 ppm;
- the growth and yield data further confirm that several plant species exhibit growth and yield effects when the mean ozone concentrations exceeded 0.05 ppm for daily 4-6 hour periods for at least two weeks;
- data from NCLAN exposure-crop response regression analyses indicated that at least 50% of the species/cultivars tested were predicted to exhibit a 10% yield loss at 7-hour season mean ozone concentrations of 0.05 ppm or less.

These findings have been confirmed in the most recent U.S. EPA assessment of yield and productivity impacts due to ambient ozone in the U.S. (U.S. EPA, 1996).

The other coordinated assessment of ozone impacts utilizing open-top chambers and chemical protectants was the European Open-Top Chamber Programme (EOTCP). Details on the findings from these studies are summarized in workshop proceedings (Ashmore & Wilson, 1993; Fuhrer & Achermann, 1994, ICP-Crops Coordination Centre, 1996).

Ornamentals

There have been a number of experimental studies designed to examine the effect of ozone on woody and herbaceous ornamental plants. Some of the herbaceous species examined include: petunia (Craker, 1972), carnation (Feder, 1970), geranium (Feder, 1970), poinsettia (Manning et al., 1973), chrysanthemum (Klingaman & Link, 1975; Brennan & Leone, 1972), turfgrass (Wilton et al., 1972) and begonia, coleus, snapdragon, marigold, celosia, impatiens and salvia (Adedipe et al., 1972). The results of these studies have shown a considerable degree of cultivar sensitivity with effects ranging from growth depression, alteration of plant habit, retardation of floral initiation as well as reductions in flower production. However, in many of these studies, ozone exposure concentrations were unrealistically high or of short duration, making extrapolation of impact to natural exposure under field conditions difficult. Even if these studies had been conducted under exposure conditions characteristic of those encountered in the field, it would be difficult to assess the economic impact of these aesthetic impacts.

Experimental progress in the case of woody ornamentals has been more advanced than for herbaceous species because many species play a dual role, being both ornamental and forest stock. As ornamentals, the majority of trees and shrubs are planted singly, exposing them fully to ambient air. This contrasts with the forest situation where a variety of canopy and stand factors must be quantified before valid extrapolations to natural settings can be made. As a result, much of the forestry oriented experimental research that has been conducted on tree seedling response to ozone has even greater value in terms of woody ornamental effects.

In a review of the tree seedling research reported up to 1986, Pye (1988) summarized ozone effects on biomass, height and photosynthesis for 43 tree species or hybrids. On the basis of this summary, and on additional work published since that time (Chappelka et al., 1988a, 1988b; Reich et al., 1987, 1988; Elliott et al., 1987; Hogsett et al., 1995; Hildebrand et al., 1996) there is convincing evidence that ozone exposures common to some areas of Canada have the potential to cause foliar injuries and growth reductions in many sensitive landscape trees.

Tree species common to Canada that have demonstrated ozone sensitivity (biomass, height, photosynthesis) under controlled ozone exposure conditions include: maples (sugar, silver, red), ash (white, green), spruce (white), white pine, poplar (hybrid), cottonwood, cherry, walnut, sycamore, white birch and red oak. Although ozone impacts varied significantly (reductions and stimulations) in many of the experimental studies, the response to seasonal mean exposures in the 40-60 ppb range for over half of the studies was reported as at least marginal growth reductions (Pye, 1988).

There is also considerable evidence that ozone can injure many annual and perennial grass species commonly used in turfgrass production in parts of Canada (Elkiey & Ormrod, 1980; Richards et al., 1980).

Forest Trees and Unmanaged Native Species

There are many different parameters and limiting factors, which must be considered in evaluating and quantifying the effects of ozone on forest trees and natural vegetation versus agricultural crops. Trees are long-lived perennial plants that are exposed to ozone repeatedly during the year over several years and, unlike agricultural crops, are not usually subjected to fertilization, irrigation, pesticide application or other cultural practices that can moderate their response in the field. Assessment of adverse effects of ozone on seedlings or young trees can be evaluated under experimental conditions; however, the large size of trees at maturity precludes experimental dose dispensing in exclusion chamber studies or the use of protective antioxidant sprays. These factors have limited the assessment of ozone impact to visual observations of foliar injury, and radial and height growth characteristics of individual trees in the stand. Where growth analysis is undertaken from different stands on the basis of air quality gradients, the data must then be considered in terms of edaphic and climatic site variation and related to ozone dose information, where available. Another complicating factor which must be addressed when assessing the overall impact of ozone on forest growth and yield is the process of inter- and intra-plant species competition and possible alterations in successional processes and species composition. In this regard, an adverse effect on the growth or survival of one tree species could have either a beneficial or detrimental effect on the growth or survival of another species, thereby increasing or decreasing the total productivity of a mixed forest stand.

On the basis of experimental chamber exposures to ozone, many tree species indigenous to eastern North America are classified as being susceptible to foliar ozone injury (Davis & Wood, 1972; Davis & Coppolino, 1974; Davis & Wilhour, 1976; Skelly, 1980). Direct injury to tree foliage by ozone has been demonstrated repeatedly in experimental situations, and in nature as well. Concentrations of ozone, at least in some forested areas, are sufficient to cause injury (Linzon, 1973; Miller, 1983; Skelly, 1980). As indicated, these ozone effects can alter the productivity, successional patterns, and species composition of forests (Smith, 1980) and enhance activity of insect pests and some diseases (Woodwell, 1970). The status of ozone-induced effects on temperate and Mediterranean forest tree species, communities and ecosystems was summarized by Skelly (1980), who concluded it is possible that primary productivity, energy resource flow patterns, biogeochemical patterns and species successional patterns may all be challenged by oxidant air pollution.

In a thorough review, Pye (1988) summarized experimental approaches, discussed tree response data from controlled fumigations and evaluated the difficulties in extrapolating experimental findings to regional, economic damage estimates.

In terms of experimental design, indoor growth chambers, greenhouses and continuously stirred tank reactors (CSTRs) have been the most commonly employed forest research technique. Outdoor exposures have used open-top chambers, branch chambers and, occasionally, chamberless designs. Although these techniques offer some control of airflow, temperature and humidity, there are still limitations in using these data for forest productivity assessment (Skärby & Karlsson, 1996; Heck & Cowling, 1997).

Before any attempt is made to extrapolate data from controlled experimental studies to the forest stand, a number of other factors must be assessed. These factors were summarized by Pye (1988) and include changes in stand regeneration, mortality, growth rates and wood quality (strength and pulp yield). Pye also points out that caution must be exercised in extrapolations based on foliar injury assessments. As was the case with agronomic species, tree growth reduction can occur without visible symptoms (Reich & Amundson, 1984, 1985; Reich et al., 1986); visible symptoms can occur without growth impacts (Jensen & Dochinger, 1974, McClenahen, 1979; Patton, 1981) and rankings of species susceptibility based on growth measures do not always correlate with rankings based on foliar symptoms (Jensen, 1973; Jensen & Masters, 1975; Kress & Skelly, 1982). This latter finding is important, since lack of growth reductions with a decreased photosynthetic area suggests compensations in carbon allocation and respiration. Another factor is the possibility that subtle growth reductions were missed due to experimental variability and inadequate error control (Wang et al., 1987) or because several seasons of exposure may be needed to demonstrate impact (Runeckles & Wright, 1996).

In his review, Pye (1988) evaluated biomass growth, height growth and photosynthesis by using data from 25 published experiments on seedlings of 43 tree species and hybrids. On the basis of these studies, it has been clearly demonstrated that ozone reduces tree growth significantly at concentrations common to many areas of the U.S. These concentrations are common throughout several areas of Canada also. Pye pointed out that in the growth response analysis, the statistical power of the study designs is a critical consideration for exposures near ambient concentrations, which are expected to result in subtle changes in plant growth. To date, problems with statistical design, genetic and environmental variability, and exposure duration have prevented the detection of significant growth reductions below about 9%. In addition to the comprehensive review of the experimental data, Pye summarized the factors that limit the extrapolation of these short-term data to longer growth cycle conditions, to mature trees and, subsequently, to stand level yield. These difficulties have been summarized below:

Extrapolating from Short-Term to Long-Term Exposures

- As trees vary in their response to and recovery from ozone over time, the length and timing of the exposure and subsequent data collection can significantly alter the experimental outcome and conclusions.
- As leaf phenology differs significantly between determinate and indeterminate tree species, the impact of ozone for a short duration will vary, depending on species type and exposure regime.
- As most conifers retain their foliage for periods well in excess of a year, the impact of a short duration ozone exposure during only part of this period is of limited value in terms of the full life-span of the foliage.

Extrapolating from Seedlings to Mature Trees

- As the balance (ratio) between metabolically active (photosynthetic) and catabolically (respiration) dominant tissues decreases with age, the impact of ozone early in the life of a tree may not directly translate into equivalent effects later in the growth cycle.
- As the micro-environment in which a leaf grows affects its morphology, resulting in large differences within a mature canopy, the impact of ozone on a uniform set of seedling leaf types may not represent the complete range of foliar response within a mature canopy.
- As water and nutritional transport and storage differ between young and old trees as cambial reserves increase, this may affect daily and seasonal patterns of stomatal conductance and influence ozone uptake and tree response.

Extrapolating from Individual Trees to Forest Stands

- As the distribution of tree sizes in a stand directly affects timber value, and as ozone impacts may directly or indirectly affect this gradient, stand volume and size distribution could be disproportionately altered; of key concern is whether stand processes will compensate for or amplify impacts on individual trees.
- As ozone susceptibility of dominant and suppressed trees within a stand will vary depending on a host of phenotypic and genotypic factors, ozone impact assessment at the stand level requires a more comprehensive understanding of stand dynamics, microclimate, genetic composition and site quality than is provided from seedling level experimentation.

A considerable body of literature has been published on forest tree seedling response to ozone since the review of Pye (1988). A recent summary of the literature prepared by Legge and Krupa (1995) identified some 17 different ozone exposure systems or protocols/methodologies used since 1985 in tree response studies. Sixty-seven citations represented experiments with 27 tree species/varieties, mostly as seedlings in chambered systems. Only four citations, two ambient exposures and two controlled ozone applications, comprised field experiments.

Duration of chambered-experiments, usually open-top, lasted from weeks up to five years in at least one case (Billen et al., 1990). One recent study (Runeckles & Wright, 1996), using a field-situated chamberless ozone exposure system, emphasized the need for multi-season experimentation in which the potential adverse effects of modest increases in ozone concentrations can be properly evaluated.

The central difficulty with respect to forest effects remains the issue of extrapolation and scaling-up of seedling data to the forest stand or ecosystem. Legge and Krupa (1995) have discussed the difficulties presented by Pye (1988) and their comparison of six general characteristics of seedlings with mature trees provides an additional level of relevant detail. The importance of changes in root morphology/function in the dynamics of carbon allocation as a tree ages cannot be underestimated, yet few data are available on below-ground response to ozone. Studies of seedlings are believed by some researchers (Samuelson & Edwards, 1993) to underestimate the sensitivity of larger and more physiologically mature trees. However, this is not yet an area of general consensus or scientific agreement.

Within a deciduous canopy, leaf position also may influence sensitivity of physiological processes. Hanson et al. (1994) noted that extrapolations of seedling-derived data to foliar responses of mature forest trees may lead to the introduction of large errors when predicting mature tree response to ozone. The definition of what constitutes a mature tree may be confounded in the case of some deciduous tree species, as ozone symptom expression was found in at least one study to be similar between overstory and sapling trees (Hildebrand et al., 1996).

In order to overcome some of the limitations which have been described for controlled environment, single species and seedling-age research, other approaches to the evaluation of ozone impacts have focused on regional scale, growth analysis studies (Ohmart & Williams, 1979; McLaughlin et al., 1983; McLaughlin, 1985; Adams et al., 1985; Cook, 1985 and Benoit et al., 1982) and evaluations of ozone levels in forested areas (Pinkerton & Lefohn, 1987). Significant ozone-related decreases in radial growth have been detected in only a few cases where ozone levels normally exceed those normally encountered in Canada and where ozone injury symptoms have been observed and documented during the past 20 years (Peterson et al., 1987; Miller, 1983). In these cases, particularly in the classic link between ozone and growth of Ponderosa pine in southern California (Miller & McBride, 1975), diagnosis of the cause of radial-growth decline was made easier by regional-scale visual changes in forest condition. Despite an apparent growth decline in large areas of the approximately 25 million hectares of southern pine forests where ozone concentrations are often elevated, diagnosis has been difficult due to the lack of a gradient in visible injury superimposed along a strong ozone gradient (Barnard et al., 1990).

Recently, however, sensitive dendrometer bands were used to elucidate the contribution of ambient ozone over five years to the seasonal growth patterns of mature loblolly pine trees in eastern Tennessee (McLaughlin & Downing, 1996). Statistically significant influences of ambient ozone on stem growth patterns were identified even though levels of ozone, rainfall and temperature varied widely over the period. Observed responses to ozone were rapid and occurred within 103 days after exposure to ozone at >40 ppb (McLaughlin & Downing, 1996). Interestingly, this response threshold is similar to that (45 ppb ozone as a 12-hour mean) suggested by Taylor (1994) for seedlings. McLaughlin and Downing (1996) concluded that relatively low levels of ozone could reduce growth of mature forest trees and that interactions between ozone and climate are likely to be important influences on future forest growth in the region. In the northeastern U.S., there is growing evidence that ambient ozone concentrations often exceed the levels that appear to cause injury for some important forest tree species (Hildebrand et al., 1996).

Definitive conclusions concerning the role of ozone in recorded growth reductions are still not possible in other, less severely impacted areas of North America due to the difficulty involved in experimental resolution and in partitioning these effects from other variables that also affect tree growth.

8.1.4 Co-occurrence Effects with Other Ambient Pollutants

Because plant life in nature is rarely exposed to the influence of only one air pollutant, extensive efforts were initiated in the mid-1960s whereby plants were subjected to combinations of ozone with sulphur dioxide, nitrogen dioxide, PAN (peroxyacetyl nitrate) and, later, simulated acid rain or fog, ultraviolet light, carbon dioxide and other components related to possible climate change. The results of these multiple exposure experiments have been classified as additive (equal to the sum of the effects of the individual pollutants), synergistic (greater than the additive effects), or antagonistic (less than the additive effects).

In 1966, Menser and Heggestad reported that tobacco plants suffered 25-38% leaf damage upon exposure to a combination of 240 ppb sulphur dioxide and 270 ppb ozone for two hours, whereas either pollutant alone at approximately the same concentrations and for the same time period caused no injury. The leaf injury caused by the combination of the two gases resembled typical ozone injury. This finding prompted an active research effort to more thoroughly determine the interactive effects and their importance to the protection of plants from ozone exposure.

Plants have been found to respond differently if the pollutant mixture regime is changed. For example, Tingey et al. (1973) found that injury on broccoli showed an additive response to a mixture of 250 ppb sulphur dioxide and 100 ppb ozone for four hours, whereas tobacco showed a synergistic response. However, if the regime was changed to 100 ppb sulphur dioxide and 100 ppb ozone for four hours, the reverse occurred, with broccoli showing a synergistic response, and tobacco an additive response.

Heagle and Johnston (1979) demonstrated another factor that must be considered in assessing multiple exposure data. They found that when soybeans were exposed to mixtures of ozone and sulphur dioxide, the response to the mixture (synergism vs. antagonism) was dependent on the concentration used. Synergistic responses were associated with low-level exposures, while antagonistic responses were documented at levels of exposure that caused more severe injury.

In another study, Runeckles and Palmer (1987) showed that sequential exposures to nitrogen dioxide and ozone could lead to different species-dependent adverse growth effects: synergistic in bean and antagonistic in radish and wheat.

Other factors that have been shown to influence the response to multiple exposures include the duration and timing of the exposure and the age and condition of the plants at the time of exposure (Mansfield & McCune, 1988).

As additional information concerning the complexity of the interpretation of multiple exposure data became apparent, research effort was aimed towards reducing the number of factorial components in the experimental technique. Ormrod et al. (1984) explored the concept of response surface techniques in studies with ozone and sulphur dioxide. This technique offers many benefits and may be further refined as work in this area progresses.

In preliminary experiments, Heck (1968a) reported that a mixture of three pollutants (nitrogen dioxide, sulphur dioxide and ozone), each at a concentration of 50 ppb, injured tobacco plants. Reinert and Gray (1981) reported that radish growth was a sensitive measure of the effects of the three pollutants in combination. Radish plants were exposed to either 200 or 400 ppb of the three pollutants alone or in combination for periods of either three or six hours. Nitrogen dioxide alone caused no visible injury, sulphur dioxide alone caused trace injury at 400 ppb for six hours, whereas ozone alone caused trace injury at 200 ppb for six hours. The exposure of radish plants to all three pollutants in combination caused greater than additive visible injury in comparison to the responses to individual pollutants or to any two-pollutant combination.

The foregoing results represent only a few of the experiments published on plant response to gaseous pollutant mixtures under short-duration, high-concentration dose regimes. Reinert (1984), Kohut (1985), Mansfield and McCune (1988), Wolfenden et al. (1992), Shriner et al. (1991), Torn et al. (1987), Ormrod et al. (1984) and Runeckles (1984) all present more comprehensive summaries and discussions of work conducted in this area over the past decade.

With increasing focus on acid rain and its precursors, and attempts to identify causal agents in a number of forest decline scenarios in the U.S. during the mid-1980s, there also was an increased emphasis on interactions involving tree seedling response to ozone, acid rain/fog, and sulphur and nitrogen oxides. Since it is not possible to thoroughly review all such efforts, the reader is directed to some of the individual studies in which these interactions were explored (Chappelka et al., 1988a, 1988b; Elliot et al., 1987; Reich et al., 1987, 1988; Stroo et al., 1988; Laurence et al., 1989; Chappelka & Chevone, 1986). As with the earlier crop research, the results of these and other multiple-exposure studies have yielded a wide range of interactions between the exposure treatments, with ozone effects being exacerbated (synergism) in many of the experiments. However, in several studies, no adverse effects or interactions were apparent. Because these studies were conducted under experimental conditions using seedling material, extrapolation or generalization to natural forest settings can not yet be made. Nevertheless, the work has focused attention on an important area since single-pollutant exposures in nature do not occur throughout the life of a tree or forest stand. The importance of this concept is underscored by the search for causality in the many forest declines that are occurring throughout areas where ozone and other regional air pollutants (sulphur and nitrogen oxides and acidic precipitation) co-exist at concentrations in the range of established threshold levels for the individual components. Clearly, until this uncertainty has been resolved, there can be no conclusive or quantitative statement regarding the magnitude of ozone impacts on forest systems.

In the area of crop yield effects, there has emerged a better understanding of the impact of ozone interactions with sulphur dioxide and acid rain/fog. In the mid-1980s, a number of seasonal crop exposures utilizing open-top chamber exposure methodologies were conducted (Takemoto et al., 1988; Kohut et al., 1987, 1988; Heggestad et al., 1986; Surano et al., 1987; Heagle et al., 1974, 1983; Temple et al., 1987; Kress et al., 1986; Reich & Amundson, 1984). In all cases, ozone in combination with sulphur dioxide and acid rain/fog at exposure levels similar to those encountered under field conditions remote from specific point sources have not resulted in enhanced yield loss above the additive individual pollutant effects. Although the field studies have not covered all crops for which ozone exposure information is available, the body of evidence appears to rule out significant interactive effects involving ozone and these major regional pollutants. However, the interaction of ozone and nitrogen oxides or the three- or four-way interaction of ozone, sulphur dioxide, nitrogen oxide and acid rain has not been specifically addressed in any of the field oriented, crop yield response research to date.

The most recent studies involving ozone interactions with other atmospheric components include the effects of carbon dioxide (climate change) and ultraviolet light (resulting from stratospheric ozone depletion). The results of these studies are still considered inconclusive in terms of interactions with ozone. A full summary of these findings can be found in Runeckles and Krupa (1994) and Krupa and Kickert (1989).

In summary, although photochemical oxidant and other co-occurring atmospheric pollution contains numerous constituents in addition to ozone, the limited amount of information available on their effects on vegetation precludes any specific estimate of the magnitude of their effects in relation to the effects of ozone alone. This finding should be considered in the light of information published by Lefohn and Tingey (1984) and Lefohn et al. (1987) who reviewed patterns of co-occurrence of ozone, SO_2, and NO_2 in urban, rural and remote sites in the U.S. during 1978-82. They found that co-occurrences were usually infrequent and of short duration. They also reported that the most frequent types of co-occurrence were usually sequential or a combination of sequential and overlapping exposures of short duration.

Because of its phytotoxic potential, PAN is undoubtedly the most important co-occurring pollutant and would not be expected to exhibit the short-duration type of co-occurrence pattern described above. However, although PAN has been documented as acting synergistically with ozone in causing increased foliar injury to some species under some conditions, this co-occurrence reaction cannot yet be generalized, as considerable variability has been demonstrated in the experimental findings published to date (synergistic, antagonistic and additive responses). Based on minimal data, that has shown relatively low PAN levels, there is insufficient information to provide a review of PAN/ozone exposure in the Canadian context.

8.1.5 Effects on Canadian Vegetation

Several studies have been designed in Canada to assess foliar injury response to ambient ozone:

- New Brunswick (Tims & Knight, 1987)
- Ontario (Pearson, 1989; Emerson, 1996)
- Quebec (Maltais & Archambault, 1985, 1986)
- British Columbia (Runeckles, 1989)

These programs have documented foliar injuries to a number of sensitive crops in New Brunswick (potato), Quebec (dry bean, soybean, tobacco), Ontario (dry bean, soybean, potato, tomato, onion, tobacco, cucumber, grape, peanut, radish) and British Columbia (pea, potato). Although these studies were not designed to determine the exposure threshold for foliar injury in all cases, injuries were observed in locations where hourly ozone levels exceeded the one-hour Canadian objective of 82 ppb for one or more hours prior to the investigation.

There have also been a number of Canadian investigations into the impact of ozone on crop yield. Using the concept of a seasonal mean as developed in the U.S. NCLAN studies as well as other U.S. and Ontario field exposure assessments via chemical protectants, Pearson (1989) determined the potential impacts (yield loss) of ozone exposure on Ontario vegetation. While the limitations of the seasonal mean exposure statistic were beginning to be recognized at that time, the lack of any generally accepted alternative index, or exposure function which could be used resulted in a decision to proceed with a seasonal mean approach. An analysis of the Ontario air quality data to assess the relationship between a seasonal mean and exceedances of an hourly criterion value of 80 ppb also was undertaken. Because the exposure-response analysis was not restricted to the utilization of field research results from the NCLAN program, and actually included many field studies conducted in Ontario for which seasonal means could be calculated, bias which would have resulted from equating crop responses to seasonal means derived from U.S. air quality data was likely reduced.

The value of increased productivity to 19 agricultural crops and ornamentals (turfgrass, Christmas trees and nursery stock) in Ontario was estimated at from 17 to 70 million dollars annually. The estimate was based on crop loss values determined from an analysis of the North American field research data (open-top chambers as well as chemical protectant studies) and subsequently adjusted downwards to reflect uncertainties in agricultural, geographical and experimental variables. The upper range represented approximately 4% of the total $1.9 billion in Ontario crop sales. Crops considered to be at greatest risk included: dry bean, potato, onion, hay, turnip, winter wheat, soybean, spinach, green bean, flue-cured tobacco, tomato and sweet corn. Crops marginally at risk (due mainly to insufficient data that did not permit more accurate quantification of loss) included cucumber, squash, pumpkin, melon, grape, burley tobacco and beet.

With the exception of Alberta (Torn et al., 1987) and British Columbia (Runeckles, 1989; Rafiq, 1989), this type of multi-crop impact analysis has not been conducted in other areas of Canada. In Alberta, the analysis consisted of a review of the available literature for ozone response based on crops grown. This information was then compared with a limited amount of urban ozone-monitoring data, and it was concluded that there were no identifiable risks to sensitive crops at that time. In British Columbia, processing peas and potato crops have been fumigated with ozone under field conditions to better define the exposure-response factors. In addition, a preliminary estimate of the crop loss due to ozone levels experienced in the lower Fraser Valley was undertaken in 1986 (Rafiq, 1989) and estimated losses at approximately $9 million. This estimate was based on a seasonal mean analysis similar to that done in Ontario (Linzon et al., 1984), but modified to reflect the longer growing seasons and milder temperatures than those in Ontario.

A brief description of the documented effects (foliar injury and yield loss) of ozone on some important field and horticultural crops in Canada follows. In many cases, this information has been compiled from visual assessment programs and chemical protectant studies conducted by various provincial agencies or research institutes. Where this information was not available from Canadian studies (either as open-top chamber studies, visual assessments or chemical protectant studies), the results of field exposure studies involving crops that normally are cultivated in Canada have been provided.

The main objective of this summary is to provide a real-world context to the impact of atmospheric ozone on ozone-sensitive crops grown in Canada and to serve as supporting evidence for the experimental findings from the U.S. and other countries that, of necessity, have been used in the exposure-response assessment. Familiarity with the symptoms affecting the various crops should also provide agencies and regulators with information to help assess the need for or effectiveness of oxidant control programs at a local or regional level.

Crops were included in the following alphabetically ordered list on the basis of investigative findings in the published literature and in internal government documents. As such, crops common to Canada but not appearing on this list should not be considered resistant to the impact of ozone—their response is simply not known at this time.

Bean, green/snap

Both acute and chronic ozone exposures of horticultural snap, bush or common beans as well as lima beans have been shown to cause foliar injury (Blum & Heck, 1980; Meredith et al., 1986). Many studies conducted under different environmental conditions, using different ozone concentrations and exposure durations, have also demonstrated the susceptibility of snap beans to ozone effects on dry matter accumulation, relative growth rate, pod production, nodulation and leaf nitrogen content. These studies are summarized in Blum and Heck (1980).

Studies of yield effects under field conditions using open-top chambers also have been conducted, although in many cases specific data on exposure parameters were not provided. In a five-year study in Maryland (1972-79), average yield reductions in non-filtered chambers relative to charcoal-filtered air chambers for snap beans ranged from 5-27% (Heggestad, 1980). Monitoring results for a nearby site in Maryland (Beltsville) were provided by Heggestad et al. (1980) and revealed that during the period from June through August, hourly ozone values equaled or exceeded 100 ppb on an average of 14 times per year. This frequency is similar to many sites in Canada.

In 1973, MacLean and Schneider (1976) detected a 26% yield loss for snap beans in unfiltered open-top chambers compared with similar plants grown in carbon filtered air. The average daily (06:00-21:00 EST) ozone concentration in the unfiltered chamber over the 43-day duration of the experiment was 41 ppb.

The most comprehensive field evaluation of ozone impact on common bean cultivars has been reported by Heck et al. (1988). In addition to the yield loss information, the authors concluded that the results provided strong support for the concept of predicting yield reduction under chronic ozone exposure (based on foliar screening results and that the NCLAN concept of comparing relative yield losses) may permit comparisons of results across seasons, years and cultivars, even though actual yields may vary greatly.

Bean, white/dry

In 1961, bronzing and rusting of white-bean foliage was reported throughout southwestern Ontario (Clark & Wensley, 1961), with yield losses in the most severely affected fields estimated at 45%. Following extensive field work in 1965 and 1967, the disorder was found to be associated with the occurrence of elevated levels of atmospheric ozone (Weaver & Jackson, 1968). The symptoms, first evident at some time between flowering and normal plant senescence, a critical period in the development of yield potential, appear as a bronze-coloured necrotic stipple on the foliage, resulting in rapid and premature leaf drop and reduced seed set as the symptoms become more severe.

The Ontario Ministry of Environment and Energy (MOEE) has conducted visual assessment surveys throughout the major production areas in southern and southwestern Ontario since 1971. Visual ratings of farm fields or experimental cultivar plantings have been made with injury severity ranging from trace (< 1%) to severe (> 35%) bronzing and associated premature foliar loss (Pearson, 1983, Emerson, 1996). These annual visual surveys have also confirmed that in any given year, the severity of bronzing symptoms was linked more with the phenological stage of the crop at the time of exposure to ozone than with varietal selection.

Experiments using chemical protectants have helped to provide information on yield losses related to the bronzing disorder in Ontario. In 1973, a 13% yield increase was associated with the reduction in bronzing severity (Curtis et al., 1975), while in 1976, yield increases of up to 36% (27% yield reduction) were realized (Hofstra et al., 1978). In 1977 and 1978 (Toivonen et al., 1982), white bean yield increases with antioxidant chemical protection were not as high (16 and 4%, respectively) and this was attributed to climatic factors (drought).

In other chemical protectant studies during 1977, 1978 and 1979 (Temple & Bisessar, 1979; Hucl & Beversdorf, 1982; Toivonen, 1980), significant yield losses were confirmed on numerous varieties across most of southwestern Ontario.

Beet

The impact of ozone on garden beet was demonstrated in a controlled exposure in California (Ogata & Maas, 1973). Ozone symptoms appeared as a fine stipple on the upper leaf surface of oldest leaves within two days of fumigation for two or three hours per day of ozone at 150 ppb. With continued exposure, the damaged areas expanded and red anthocyanin-like pigment in the interveinal areas turned a dark purple. In advanced stages, the interveinal areas became necrotic and desiccated. Significant reductions in storage root weight were recorded with exposure durations in excess of one hour per day. In a more recent California study (McCool et al., 1987), using closed-top field chambers with a 12-hour seasonal mean ozone statistic (9 ozone concentration regimes), yield reductions of 6.6 and 11.1% were calculated from a linear model for 12-hour seasonal means of 40 and 50 ppb, respectively.

Cucurbits (Cucumber, Squash, Melon, Pumpkin)

Chlorotic mottle of leaves, early leaf senescence, and possibly increased susceptibility to diseases are problems incurred by cucurbit species in southern Ontario each year due to oxidant exposure (Ormrod, 1980). In 1979 and 1980, studies were undertaken to assess the relationship between foliar symptom development and yield suppression in cucumber. The studies utilized a number of different locations using two different chemical protectants. The results (Ormrod, 1980, 1981) revealed that at some locations there was a cultivar response to chemical protection. The results in 1979 were less conclusive than those of 1980, when overall reductions of 13% were recorded, with one location (all cultivars) yielding 15% less in unprotected cucumber plots compared to those provided with antioxidant protection.

Studies on muskmelon and watermelon in Indiana also have confirmed the role of ozone in extensive foliar injury development and reduced fruit yield (Snyder et al., 1988; Eason et al., 1986). In open-top chambers with and without carbon filtration, significant yield reductions of

21.3 and 20.9% for marketable fruit weight and fruit number were documented for "Superstar" muskmelon (Snyder et al., 1988).

Grape

Dark brown to black spotting or stipple of grape leaves was first reported in California (Richards et al., 1958) and attributed to the presence of atmospheric ozone in the grape production areas. The symptoms, which include premature leaf senescence and abscission, are commonly called 'brown leaf disorder'. These symptoms reportedly are widespread on several American cultivars and French hybrids grown in vineyards throughout upper New York state (Shaulis et al., 1972). In 1973 and 1974 (Kender & Carpenter, 1974), a large number of grape cultivars and hybrids in both New York state and Ontario was assessed for severity of oxidant injury.

These findings prompted a four-year Ontario study to ascertain the extent of the problem in terms of the severity of foliar injury development and potential adverse effects on crop yield and quality. These results (Ormrod, 1979) confirmed that the 'brown-leaf' disorder of grapes is a readily recognizable problem in Ontario each year. The failure of the antiozonant chemical treatment to provide sufficient protection from foliar injury development negated the efforts to quantify any adverse yield and quality effects. In California, however, adverse yield and quality effects were demonstrated, using Zinfandel grapes in field studies with protection by charcoal-filtered chambers (Thompson & Kats, 1970).

In a review of air pollution effects on grape vines, Weinstein (1984) summarized the available research and concluded that losses in fruit yield and quality can occur in the field at ambient ozone concentrations, with some cultivars exhibiting extreme susceptibility while others demonstrated remarkable tolerance. However, most observations have been associated with foliar lesions and the relationship between these symptoms and fruit yield has not been well established.

The work of Musselman et al. (1985) in New York, using the Concord cultivar with mature vines in open-top chambers, confirmed the conclusions drawn by Weinstein (1984). The exposure of the crop to ambient ozone in combination with different dose regimes of sulphur dioxide revealed that intermittent exposures of sulphur dioxide reduced foliar tolerance of ozone. There were no significant effects, however, of one or two years of ambient air filtration (ozone reduction) on vine yield, growth, maturity or soluble fruit solids.

Hay

Compared with annual crops, relatively little information is available on multi-year yield responses of perennial forage crops to ozone (Temple et al., 1988).

Under controlled environmental conditions, Brennan et al. (1969) evaluated the foliar response of numerous forage legumes and found that sensitivity increased in the following order: crown vetch > alfalfa > alsike clover > white sweet clover > red clover.

In the case of clover, ozone has been shown to reduce the yield, inhibit nitrogen fixation, shift the grass/clover yield ratio in favour of the grass and accelerate the loss of clover from the combination (Blum et al., 1983). In another study, Blum et al. (1982) also reported that ozone suppressed root growth and reduced total non-structural carbohydrate reserves in roots and shoots of clover. Other studies involving the exposure of clover to ozone are summarized in reviews by Ensing and Hofstra (1982), Kochhar et al. (1980) and Bennett and Runeckles (1977).

In California, Middleton et al. (1950) estimated that 15% of the alfalfa crop was lost due to air pollution exposure in 1949. Oshima et al. (1976) also used alfalfa in California to assess the impact of ozone via controlled, containerized studies across an ozone gradient. Other studies that review the impact of ozone on alfalfa include Cooley and Manning (1988) and Olszyk et al. (1986, 1988).

Onion

Onion leaf dieback and flecking have been attributed to a number of parasitic and non-parasitic agents since the first report of the disorder in Wisconsin in 1903 (Whetzel, 1904). Subsequently, the search for the causal agent in the tip-burn or blast syndrome centred on atmospheric ozone. Engle et al. (1965) found a close relationship existed between the presence of flecking and tip-burn in onions and high levels of ozone. Engle and Gabelman (1966) later published on the genetic resistance of certain cultivars of onions to ozone exposure.

In Ontario, Wukasch and Hofstra (1977a, 1977b) examined the effects of ozone exclusion and chemical protection on the yields of field-grown onions. They documented a 28% yield reduction in non-filtered compared with charcoal filtered chambers, and a 22% yield reduction in control plants (Autumn Spice) compared with those provided with an antiozonant protectant. Another cultivar (Rocket) failed to confirm these significant protectant effects.

In a later California study, using closed-top field fumigation chambers, McCool et al. (1987) demonstrated a significant yield loss for green bunching onions exposed to various 12-hour seasonal mean ozone concentrations. The linear response model predicted yield losses of 14.9% and 24.8% for seasonal means of 0.04 and 0.05 ppm ozone using the 12-hour seasonal mean statistic.

Potato

The foliar symptoms referred to as 'speckle leaf' on this crop usually appear after mid-July when the plant has flowered and the tubers are developing. As the demands for photosynthetically produced nutrition at this time are at their peak, the potential for adverse yield effects is considerable. The symptoms appear either as a blackened stipple or flecking on the upper leaf surface which can coalesce and become bifacial necrotic lesions; or as undersurface, irregularly sized, silver-grey lesions, which also can become bifacial as they increase in size and severity. Adding to the total impact of this injury are findings (Bisessar, 1982; Holley et al., 1985) which demonstrate that ozone injury predisposes the plants to attack by the early blight disease organism, thereby necessitating additional disease control treatments.

In Ontario, ozone induced foliar symptoms were observed as early as 1954 (Johnson, 1972) and in later years (McKeen et al., 1973). On the basis of yield assessment studies conducted in Ontario and in northeastern U.S., yield losses and tuber quality effects have been documented on several of the most sensitive processing cultivars. In Ontario, Ministry of Energy and Environment (MOEE) also has conducted annual foliar injury assessment surveys throughout the major potato production areas since 1977 and in that time have examined over 600 plantings and recorded foliar injury development ranging from less than 1 to 30% leaf area (Pearson, 1983; Emerson, 1996). Foliar injuries have also been reported in New Brunswick and British Columbia.

In studies using antioxidant protective chemicals, potato (Norchip) yield losses in Ontario with and without disease control were 24.2% and 26.2%, respectively (Bisessar, 1982). An average, significant yield loss of 8.2% in an ozone sensitive cultivar (Norchip) also was reported during a three-year trial in Ontario (Holley et al., 1985). This loss could be attributed to ozone effects that were apparent under a disease control program; no demonstrated yield effects were detected with two other, more ozone resistant cultivars (Chieftan and Kennebec) in the same trial (Holley et al., 1985). The trials, which used chemical protectants, are comparable to open-top chamber studies undertaken in 1986 (Pell et al., 1988). Pell et al. (1988) also demonstrated significant tuber quality effects. Another open-top chamber study conducted earlier in California (Foster et al., 1983) confirmed a linear exposure-response to season-long ozone exposures in terms of tuber number and total tuber yield. Runeckles et al. (1990) observed a response similar to that found by Foster et al. (1983) as a result of season-long exposures to ozone in an open-air field fumigation system.

On the basis of these studies as well as general reports of foliar injury and/or yield losses in northeastern and southwestern U.S. (Mosley et al., 1978; Hooker et al., 1973; Foster et al., 1983) and a documented 50% loss to a sensitive variety under greenhouse conditions (Heggestad, 1976), there is convincing evidence that this crop is reduced in yield by ozone exposure scenarios similar to those experienced in several parts of Canada. An assessment of potato yields from 1941-94 throughout Ontario (McKeown, 1996) has demonstrated that yields which had been increasing until the early 1960s then leveled off and began to decline in the 1970s. Potato experts are concerned that this trend is occurring despite newer varieties, better pest control, extra fertilizer, irrigation and soil fumigation.

Soybean

In the early 1970s, some greenhouse studies documented the foliar response of a number of soybean cultivars to acute and chronic doses of ozone (Heagle, 1979; Howell & Kremer, 1972; Tingey et al., 1972). It was later demonstrated (Heagle & Letchworth, 1982) that neither foliar injury nor the vegetative shoot weight response of cultivars to ozone allowed reasonable prediction of cultivar yield response. At the end of the decade, studies confirmed crop yield losses under field conditions using open-top field chambers equipped with ozone filtration devices (Heagle & Heck, 1980; Kohut et al., 1977). These studies underscored the need for more accurate assessments of yield effects utilizing open-top chambers with supplemental ozone additions (Kress & Miller, 1983). During this period of active NCLAN supported and independent research, a number of investigations employing a variety of potentially interactive variables—sulphur dioxide, acid rain, soil moisture—were conducted.

With the exception of the chemical protectant studies (Smith et al., 1987; Brennan et al., 1987) and an earlier open-top chamber study (Howell et al., 1979), the experimental yield losses from the various controlled exposure studies (Kohut et al., 1986; Reich and Amundson, 1984; Heagle et al., 1986, 1987b) revealed a fairly uniform degree of plant response, considering the potential influences of location, exposure dynamics, cultivar, soil moisture and other environmental variables.

Because of its ozone sensitivity and importance to U.S. agriculture, soybean has been the primary focus in the experimental study of ozone-soil moisture interactions and the development of predictive moisture stress models for crop loss assessment (Heggestad et al., 1985, 1988; Heagle et al., 1987; King et al., 1988; King & Nelson, 1987). On the basis of this work, King and Nelson (1987) predicted a 23% decline in sensitivity of drought-stressed plants to ozone based on a 1980 U.S. ozone exposure scenario. For the period 1979-83, the mean predicted ozone impact on soybean yield was 19% less when the plants were under moisture stress, than was predicted for adequately watered soybean-yield.

Spinach

Several studies have documented the impact of ozone on spinach plantings (Daines et al., 1960; Manning et al., 1972) and confirmed cultivar response variability and typical short-term acute foliar symptoms. Heagle et al. (1979a) reported on the first growing season exposures, conducted in 1976, to determine whether spinach cultivars vary in sensitivity and to establish threshold doses of ozone for injury and decreased shoot weight. The authors confirmed that under seasonal exposure regimes, the foliar symptoms resembled those described for acute exposures; however, the major symptom was chlorosis, as opposed to bifacial necrosis. There were no relationships between foliar injury and shoot fresh or dry weight.

Sweet corn

In the first report ever to demonstrate yield loss in an agronomic crop exposed to long-term, low levels of ozone under field conditions using field exposure chambers, Heagle et al. (1972) evaluated the response of two cultivars of sweet corn (Golden Midget and White Midget). Ozone injury was described as small white or tan adaxial necrotic spots plus early chlorosis and senescence on the lower leaves. Growth reductions were not proportional to injury severity.

In California, Thompson et al. (1976) used open-top field chambers with and without carbon filtration and demonstrated foliar symptoms similar to those reported in other studies. Both cultivars (Monarch Advance and Bonanza) were seriously injured in ambient air; however, growth and yield parameters were more significant for Monarch Advance, with the greatest response being an effect on number and quality of seeds set on primary ears.

Tobacco, burley

Weather fleck of tobacco, so named because of its relationship to certain weather conditions, has been recognized as an ozone induced foliar disorder in Ontario since 1954 (Cole & Katz, 1966). Weather fleck has also been recognized as a factor in the production of tobacco in Quebec (Maltais & Archambault, 1985, 1986). The symptoms appear on newly expanded leaves, the younger and older leaves being more resistant. Symptoms normally first appear on the upper leaf surface as greyish, water-soaked lesions that become light ivory to tan-brown in colour with time. In more severe episodes the lesions can coalesce into larger flecks or spots and become bifacial with increasing severity. Successive episodes of ozone fumigation result in new lesions appearing on healthy tissues of recently injured leaves as well as newly expanded leaves higher on the main stem.

Weather fleck results in moderate damage to the burley tobacco crop in southwestern Ontario each year (Anderson & Welacky, 1983). The loss is attributed to the shattering of flecked leaves during curing and stripping operations. There is also potential for adverse effects on quality since chemical characteristics are affected (Huang et al., 1976; Menser et al., 1977). In 1980 and 1981, visual estimates of weather fleck damage on 13 burley cultivars at Harrow, Ontario, revealed mean damage on leaves 1-12 ranging from 3.0 to 7.2% in 1980 and 0.2 to 9.4% in 1981 (Anderson & Welacky, 1983).

Tobacco, flue-cured

Although considerable success has been achieved in breeding ozone resistance into commercially acceptable tobacco cultivars, yield losses associated with this crop continue to affect tobacco production (Ormrod et al., 1980; Watson & Sheidow, 1982). In 1972 and 1973, Gayed and Watson (1975) estimated decreased leaf weight and quality effects of 0.73% while estimates of tobacco crop loss in Ontario for the years 1975-81 varied from 0.2-2.5% (Watson and Sheidow, 1982). An MOEE visual assessment of foliar injury severity consisting of 33 separate observations throughout the major tobacco production areas of southern Ontario in 1977 confirmed the presence of foliar injury development ranging from < 1 to 20% on flue-cured tobacco species (Pearson, 1983).

Tomato

Tomato is an ozone sensitive crop species and has been investigated for cultivar sensitivity (based on foliar injury) by a number of researchers. Typical injury symptoms are frequently reported in the field in Ontario (Pearson, 1983).

There are numerous reports which document the adverse effect on tomato yield due to ambient (MacLean & Schneider, 1976; Oshima et al., 1977; Heggestad et al., 1986; Heck et al., 1984b) or controlled environment exposure (Henderson & Reinert, 1979). In North Carolina, early marketable yield of some tomato cultivars was significantly reduced by exposure of the plants to ozone prior to their establishment in the field (Henderson & Reinert, 1979). In spite of the fact that the final total yield was not affected, an economic loss was predicted based on the price differential between the early- and late-season markets. In a New York study, MacLean and Schneider (1976) documented a 33.7% yield reduction effect for plants grown in unfiltered chambers relative to charcoal-filtered chambers. The calculated average seven-hour seasonal mean in the filtered chamber over the duration of this experiment was 22 ppb ozone while that in the unfiltered chamber was 63 ppb.

As part of the NCLAN study, yield loss with Murrieta tomato in California (Surano et al., 1987) was estimated at 2.4 and 7.5% for seasonal seven-hour exposures of 40 ppb in 1981 and 1982, respectively, and 4.9 and 14.4% at 50 ppb in 1981 and 1982, respectively. Heggestad et al. (1986) reported a 16.3% yield loss for Jet Star using filtered versus unfiltered open-top field chambers in Beltsville with a calculated seven-hour seasonal mean of 50 ppb compared to 15 ppb in filtered chambers.

There are two Ontario reports citing an adverse effect of ozone on tomato yield. Legassicke and Ormrod (1981) record a yield reduction of 23.7% for one cultivar compared with tomato plants afforded chemical protection. Ormrod (1983) found reductions in tomato yield for several cultivars at several locations in both 1980 and 1981. Although many of the cultivar comparisons were not statistically significant, there were some that approached 30% yield reduction.

Turnip

Significant yield losses have been documented for this crop. At Raleigh, foliar injury appeared as chlorosis on cotyledons followed by chlorosis of a few of the oldest true leaves. After one 3.5-hour acute episode during late November, there were water-soaking symptoms apparent on expanded leaves of all cultivars (Heagle et al., 1985).

A California study (McCool et al., 1987) conducted under significantly different climatic conditions using closed-top field chambers and a 12-hour seasonal ozone exposure duration, obtained yield response very similar to that in Raleigh.

Winter wheat

Until recently, little was known about the impact of season-long ozone exposure on the yield of winter wheat. The work of Shannon and Mulchi (1974) and Sechler and Davis (1964) had indicated that wheat was sensitive to short-term acute exposures at anthesis under controlled-environment and greenhouse conditions and that, to a limited extent, cultivar differences were apparent. In 1978 and 1979, Mulchi et al. (1986) conducted field experiments in Maryland using open-top chambers and six cultivars of soft red winter wheat. Although the ozone exposure was not expressed in a seasonal format, all six cultivars exhibited susceptibility to ozone injury during anthesis. In an earlier field experiment (Phillips & Runeckles, 1974), wheat biomass was reduced with exposure to five-hour-per-day concentrations ranging from 80 to 100 ppb. Yields were not reported.

In later NCLAN studies (Kress et al., 1985; Kohut et al., 1987) utilizing both constant and proportional ozone exposures, significant yield losses were recorded for both soft and hard winter wheat cultivars. In the latter study, ozone was shown to accelerate senescence of flag leaves and heads, with reductions in yield being highly correlated with reductions in net photosynthesis (Amundson et al., 1987).

Crops with limited experimental results

Foliar injury and yield loss have been documented for a number of other crops grown in Canada, including: radish, pea, carrot, celery, cabbage, cauliflower, eggplant, pepper, sunflower, peanut, field corn, strawberry, spring barley, oats and apple. In the case of celery, pepper, strawberry, spring barley, field corn and leaf lettuce, studies have used either open- or closed-top chambers with constant or proportional ozone dispensing under field conditions (Takemoto et al., 1988; Temple et al., 1985; Heagle et al., 1979b; Kress & Miller, 1985; McCool et al., 1987). Runeckles et al. (1990) reported yield losses of processing peas as a result of season-long exposures in an open-air field fumigation system.

Sensitivity to ozone also has been demonstrated for the other crops; however, except for peanut (Ensing et al., 1985), the experimental studies have been limited to short-duration, foliar-effect or biomass evaluations which do not permit an assessment of yield impact under field conditions. The peanut study in Ontario did document an adverse impact on yield, but this was limited to one of several cultivars tested using chemical protectants.

Forest Trees and Unmanaged Vegetation

Ozone concentrations are elevated in forest areas within portions of four Canadian terrestrial ecozones: Atlantic Maritime (New Brunswick, Nova Scotia, Prince Edward Island), Mixedwood Plain (southern Quebec, southern Ontario), Pacific Maritime (Lower Fraser Valley, British Columbia) and, to a lesser extent, the Boreal Shield (southwestern Ontario). In these areas, ozone concentrations exceeded the current NAAQO of 82 ppb for between 10 to 50 hours per year during 1986-93 (Environment Canada, 1996).

In Ontario, foliar symptoms associated with ozone injury to white ash and eastern white pine have been observed by MOEE staff. Reductions in radial growth of a number of hardwood species also have been documented throughout these areas (MOE, 1989). However, until such time as additional studies are undertaken, the role of ozone in these documented forest growth reductions cannot be confirmed or quantified.

On the east coast along the 600-km Bay of Fundy-Gulf of Maine transect, declines of white birches and red spruce occurred in the 1980s. This area receives some of the most acidic fogs and has recorded among the highest hourly ozone concentrations in North America, with the exception of southern California (Jagels, 1986). Although ozone may have been an important interacting factor (Cox, Spavold-Tims & Hughes, 1989), foliar injury to birches (Cox, Lemieux & Lodin, 1996) and changes to red-spruce needle-surface properties (Percy et al., 1993) were related directly to fog frequency and chemistry. Field observations on declining red spruce trees confirmed or were later supported by ozone and acid fog experimental exposures using red spruce seedlings (Percy et al., 1990; Percy et al., 1992) or recrystallized needle waxes (Percy et al., 1992).

8.2 QUANTITATIVE TOXICITY ASSESSMENT

8.2.1 Experimental Methodology to Assess Crop Response

With the recognition in the late 1970s and early 1980s that foliar injury resulting from short-term, acute fumigations may not adequately characterize the season-long, chronic effects of ozone exposure on crop and forest yield or biomass production, a number of techniques have been developed to facilitate a more accurate, quantitative assessment of ozone impacts under conditions more typical of field exposure. A review of the various approaches to experimental field exposures in examining ozone-induced crop loss is summarized in Table 8.2. A detailed description of the individual exposure methods can be found in Hogsett et al. (1987a, 1987b).

Among all field exposure methods, the open-top chamber approach has been the most frequently used and accordingly has formed the basis for the exposure-response assessment summary that has been undertaken in this document. This section, essentially extracted from Manning and Krupa (1992), provides additional detail on the open-top chamber methodology.

In response to the observed excessive increase in daytime temperature and the lack of exposure to ambient rainfall in closed field chambers, Heagle et al. (1973) and Mandl et al. (1973) developed large cylindrical open-top chambers (OTCs). Charcoal- or dust-filtered ambient air is blown into the bottom of the OTC at a velocity that permits it to rise within the chamber and exit through the open top. This reduces ingress of ambient air from above the OTC and prevents problems with daytime increases in temperature. In addition, ambient rainfall enters through the open top. The Heagle OTC design (Heagle et al., 1973) has been the one most frequently used for more than 20 years, including the U.S. Environmental Protection Agency's National Crop Loss Assessment Network (NCLAN) (Heck et al., 1982, 1984a, 1984b, 1988; Heagle et al., 1988). Similar OTCs have been used to study ozone effects on plants as diverse as cereals, grapevines and large trees. Design variations in OTCs have been described in detail by Hogsett et al. (1987a, 1987b) and Last (1986). With the addition of a rain cap, OTCs can also be used to study precipitation effects and soil moisture regime interactions (Hogsett et al., 1985).

Table 8.2 Summary of field exposure systems used to assess ozone effects on crops.

Systems	References
Open-air plumes [Circular, grid, linear, square, zonal air pollution system (ZAPS)]	Lee and Lewis (1978), Greenwood et al. (1982), Thompson et al. (1984), McLeod et al. (1985), Runeckles et al.(1990).
Air pollutant exclusion	Jones et al. (1977), Shinn et al. (1977), Olszyk et al. (1986a, 1986b).
Linear gradients	Shinn et al. (1977), Laurence et al. (1982), Reich et al. (1982), Olszyk et al. (1986a, 1986b)
Field chambers Closed chambers	Roberts (1981), Ashenden et al. (1982), Musselman et al. (1986)
Down-draft chambers	Runeckles et al. (1978)
Open-top chambers	Mandl et al. (1973), Heagle et al. (1973, 1979), Nystrom et al. (1982)

Source: Modified from Manning and Krupa, 1992

Under conditions of low wind velocity, the charcoal filters may remove 50-60% of the ambient ozone. Downdraft incursions of ambient air into the OTCs increase with wind velocity, potentially causing problems in meeting specified treatment levels. Several designs involving additions of a baffle or frustum to the top portion of the OTCs have been evaluated to reduce downdrafts (Kats et al., 1976; Kohut et al., 1978; Davis & Rogers, 1980; Buckenham et al., 1981). The use of a truncated, cone-shaped frustum (Kohut et al., 1978) increases the removal efficiency of ambient ozone to 75% (Davis & Rogers, 1980). However, the advantages gained in ambient air exclusion are off-set by reductions in the ingress of ambient rain and solar radiation. However, the uniformity of distribution of introduced ozone within the OTC is increased (Davis & Rogers, 1980).

OTCs have been used for many years, allowing the accumulation of considerable information about their performance under a variety of conditions. Some advantages and disadvantages of the use of OTCs are summarized in Table 8.3. More extensive consideration of OTCs has been provided elsewhere (Krupa, 1984; Unsworth et al., 1984a, 1984b; Hogsett et al., 1987a, 1987b; Heagle et al., 1988; Ormrod et al., 1988; Heagle, 1989; Krupa and Nosal, 1989a).

OTCs were originally used to compare crop responses to CF (charcoal filtration) and NF (non-filtered, i.e., particle and dust filtration only) treatment under field conditions (Heagle, 1989). CF treatments were intended to remove ozone from the air in the OTC, while NF treatments were controls. CF was found to increase yields of crops such as bean, cotton, field corn, peanut, potato, soybean and wheat when comparisons were made with yields from NF. This allowed determination of possible ambient ozone effects on crops in any given area. Results varied from year to year as weather conditions and ambient ozone concentrations and exposure patterns varied.

Table 8.3 Advantages and disadvantages in the use of open-top chambers

Advantages	**Disadvantages**
Widely used with 15+ years of historical records, especially for CF/NF comparisons	Problems with comparison of results from CF, NF and AA
Crops can be grown to maturity in the field	Limited space in chambers; long-term use may mask effects in perennial plants and trees
Exposure-response studies at concentrations above ambient can be made by ozone additions	Microclimate effects may affect results (e.g., soil moisture problems, changes in insect and disease incidence)
Each OTC is cost effective, portable and durable	The many OTCs required for field work are expensive and labour-intensive; each chamber requires a 20-amp circuit
	Use leads to increased plant growth in cool seasons and winter compared to AA plants

Source: Manning and Krupa, 1992

Proportional or fixed concentrations of ozone, separately or in combination with other pollutants can be added to OTCs. This allows exposure-response studies in the field, with a range of concentrations of ozone above ambient levels (Heagle & Philbeck, 1979; Heagle et al., 1979; Heagle, 1989). Hogsett et al. (1987a, 1987b) and Nystrom et al. (1982) developed computerized systems to maintain OTCs and dispense ozone in a pattern that simulated fluctuating ambient air concentrations. Data from OTC exposure-response studies have been used to predict how changes in future, elevated ozone concentrations will affect crop yields.

Chamber effects have been intensively investigated and described in detail by Musselman et al. (1978), Olszyk et al. (1980, 1989), Weinstock et al. (1982), Ashmore et al. (1988), Colls et al. (1988), Heagle et al. (1988), Manning and Keane (1988), and Heagle (1989). A condensed summary of chamber effects, based on all of the previously cited work, is presented in Tables 8.4 and 8.5.

Howell et al. (1974) expanded the CF versus NF experimental approach to include comparisons with a comparably sized, non-enclosed ambient air (AA) or chamberless plot. Results from CF, NF and AA are not be directly comparable due to the composition of the air that plants are exposed to as a result of CF, particle (dust) filtration (NF), ambient air (AA), chamber and no chamber. An important consideration in such analyses involves an understanding of the type of charcoal used for filtration. Different types of charcoal provide different degrees of filtration of different pollutants. Nystrom et al. (1982) have used this feature to advantage in their differential studies on ozone, SO_2 and ozone + SO_2. Most recently, Olszyk et al. (1989) examined air composition in CF and NF and AA in the South Coast Air Basin in California and compared the efficiency of charcoal and particle filters. Concentrations of NO in CF were higher than in NF and AA, probably due to conversion of NO_2 to NO on the charcoal filter. Concentrations of ozone, NO_2, PAN, NO_3, S_2O_4, and NH_4+ were greatly reduced by charcoal filtration. To the contrary, plants in NF were exposed to near-ambient concentrations of ozone, NO_2 and PAN.

OTCs are useful in assessing ambient ozone effects on crops and simulating ambient effects, using comparisons between CF and NF as long as sufficient numbers of replicate chambers are used to provide adequate power for the statistical comparisons that are planned (Rawlings et al., 1988). Exposure-response studies with elevated ozone concentrations added to CF and NF can also be accomplished with OTCs. However, problems may develop when comparisons are made among CF, NF and AA. Chamber effects should always be investigated in a systematic way in order to determine their influence on plant responses in the CF and NF chambers. It is apparent that at a minimum, this analysis should include an assessment of differences in results between NF and AA.

Table 8.4 Effects of open-top chambers—physical changes

Physical parameters	Changes observed
Air filtration effect	
Activated charcoal (CF)	50-75% reduction in ambient ozone, increase in NO over ambient, and considerable reductions in NO_2, PAN, and SO_2
Particles (dust) (NF)	5-10% reduction in ambient ozone, some reduction in SO_2
Gas Exchange	
Canopy resistance	Similar to ambient air
CO_2 uptake	Inconsistent effects
Leaf boundary layer resistance	Less in OTCs
Stomatal conductance	Variable
Microclimate	
Air turbulence	Greater in downwind half of chamber
(due to ingress of ambient air)	
Dewpoint	0.5-2.0°C higher.
Light	Decrease of 12-20%, especially with dirty plastic, sun shadows possible
Relative humidity	5-10% increase or decrease
Temperatures	
Air	2.0-3.7°C increase
Leaf	Slight increase
Wind speed	Decrease

Source: Manning and Krupa, 1992

Table 8.5 Effects of open-top chambers—biological changes

Biological factors	Changes observed
Microclimate effects (not defined)	Plants in NF may yield less than in AA Plants in NF are often taller than in AA Chambers can delay leaf senescence and shorten maturity in grapevines
Pesticide usage (usually increased)	Unusually low occurrences of disease, insects and mites
Pollination problems	Fewer bees in chambers reduces seed pod set and seed yields in broad beans
Position effects in chambers	Higher yields may occur in northern rather than southern half of chambers

Source: Manning and Krupa, 1992

8.2.2 Form of an Exposure Index for Chronic Effects

One of the critical issues facing modellers of ozone exposure-plant response relationships is to understand how ambient concentrations of ozone are experienced by the plant. In other words, how does the dose taken up by the plant relate to ambient concentrations, and what factors and meteorological conditions are critical in determining the dose? These considerations have led to the separation of the concept of dose into the terms 'exposure dose' (Krupa & Kickert, 1987a) and 'effective dose' (Runeckles, 1974). 'Exposure dose' may be defined as the air concentration and exposure duration to which the plant is subjected. 'Effective dose' may be defined as the actual concentration over time absorbed by the plant. While most current ozone effects models use a numerical expression of exposure dose, the evaluation and use of the effective dose is a very important future need, particularly in terms of predicting the magnitude of plant response from a given set of air quality data. Runeckles (1992) provides a thorough discussion of 'effective dose'.

A logical follow-up to the discussion above is a review of some concepts relevant to ambient ozone exposure dynamics and plant response. In a Weibull distribution of ambient ozone concentrations, the left portion of the distribution represents background ozone concentrations while the right portion of the distribution tail represents the occurrences of ozone episodes. While the occurrence of ozone episodes may be viewed as periods of stress, depending on the tolerance capacity of the plant and the nature of the other prevalent environmental conditions, periods of non-ozone episode days should be viewed as opportunities for repair or compensatory growth for the plant, providing that other conditions (i.e. water, light, nutrition) are favourable (see section 8.1).

Repair and compensation in response to low concentrations of ozone is largely a conceptual model based on a limited understanding of plant energy budgets. It is known that enzyme systems responsible for detoxifying oxidant species in cells require energy to function. As well, reactions between oxidant species and photosynthetic enzymes will reduce the amount of carbohydrates available for mitochondrial energy production, as well as for structural growth components. In an energy budget with no elasticity, either of these diversions of energy would be expected to reduce plant growth or yield. However, it is well accepted that energy budgets are elastic and plants may reallocate resources among various sinks to compensate for stress effects on a particular sink. Minor reallocations in response to low levels of stress may be accommodated within the elasticity of the plant, with no net effect to the plant or at least not of a magnitude that can be detected. Larger reallocations in response to greater stress may ensure survival, but with some net loss which is detectable. Depending on concentration and duration of exposure, the effect on the plant could be a negligible, minor or major reallocation of energy among plant parts or sinks. It is important to note that the concepts of repair/respite/compensation are not yet quantified, nor have the benefits of various characteristics of respite time been satisfactorily addressed, hindering the ability to model plant responses.

In recent years, one of the most frequently used terms in defining ozone exposure-crop and response relationships is 'exposure index or indices' (Heck et al., 1988). The concept of 'dose' forms the basis for the use of an exposure index or indices. The objective is to identify one or more ozone exposure parameters that can satisfactorily explain cause-effect relationships. The exposure index or indices also must demonstrate a generality and a universal applicability (Lefohn et al., 1989) and serve both as an assessment and predictive tool.

The relative importance of peak vs. mid-level ozone concentrations

According to Lefohn (1994), in a review of ozone exposure indices, the establishment of an ozone exposure index to predict vegetation response to ozone should consider the following:

- higher hourly average concentrations should be given more weight than the lower values and concentration is more important than duration in predicting vegetation effects (U.S. EPA, 1986, 1992; Hogsett et al., 1988; Lefohn, 1992);
- an index may attempt to protect vegetation from a) injury (measurable responses that do not influence agronomic yield or reproduction) or b) damage (all effects that reduce the intended human use or the value of the plant or ecosystem) (Tingey et al.,1990);
- hourly concentrations ≥0.10 ppm in the exposure regimes for most of the 22 NCLAN experiments resulted in a 20% yield reduction (Lefohn & Foley, 1992); Guderian et al. (1985) also noted the importance of hourly average concentration of ≥0.10 ppm in predicting plant response.

A number of investigators have used statistical regression techniques to identify numerical descriptors of ozone exposure that may best explain/predict crop response (Lee et al., 1988;

Lefohn et al., 1988; Tingey et al., 1989; Musselman et al., 1988, Hogsett et al., 1988, 1995). The coefficient of determination (R^2) and the residual mean sum of squares (RMSS) in the regression between various air quality indices and plant response have been used as criteria for evaluating the comparative efficacy of various exposure indices in establishing ozone exposure-crop response relationships

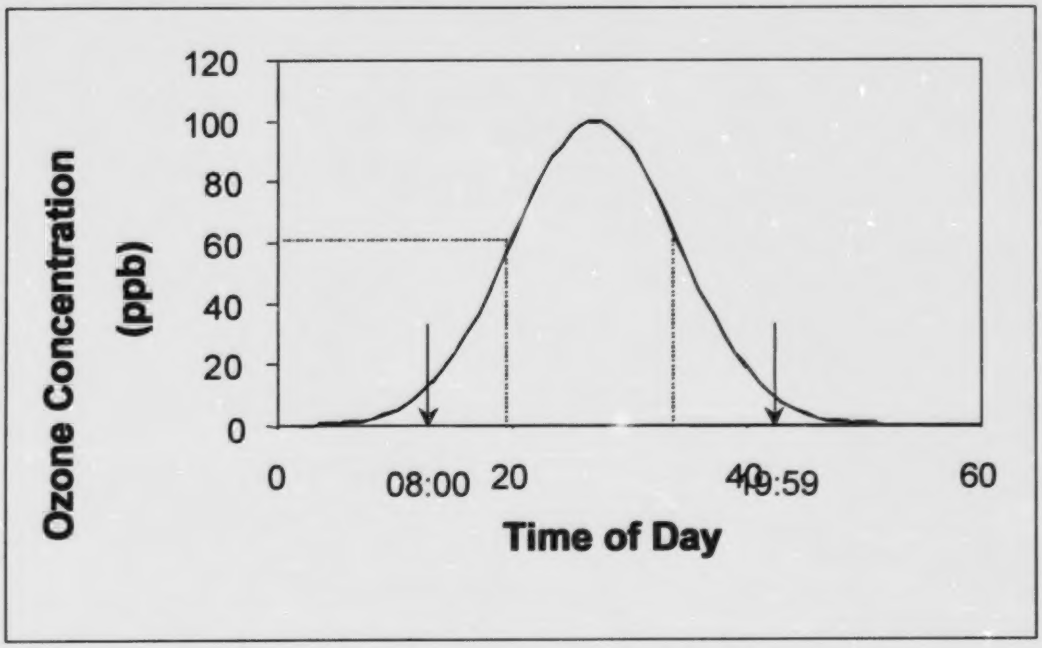
Based on the evaluation of over 500 different forms for a crop response index of ozone air quality, the findings of several scientists were summarized by Lee et al. (1988). This analysis pointed to the following factors as major considerations in the development of exposure indices:

- peak concentrations are more important than low concentrations in determining plant response;
- temporal distribution and intensity of concentrations over the exposure period need to be included;
- changes in exposure structure alter the magnitude of response;
- ozone effects increase with increasing duration of the exposure period although the exposure-response relationships are rarely linear;
- exposure cannot be characterized as the product of concentration and time since the effect of ozone on crop yield depends on the cumulative impact of high concentrations during the growing season
- plant sensitivity is not constant, but varies according to stage of development;
- time of increased plant sensitivity is species-specific, but generally occurs at or near maximum leaf expansion.

Considering these and other related ozone index development efforts, the authors concluded that the effects of ozone are cumulative and that higher concentrations are more important than lower concentrations in determining plant response. Accordingly, they believed that the form of a standard to protect vegetation should be cumulative (summation of hourly values) and should emphasize peak concentrations.

Two forms of exposure indices that performed the best in terms of statistical relationships with crop yield were the SUM60 and the sigmoidally weighted indices. The SUM60 index is calculated by summing hourly ozone when concentrations are equal to or greater than 60 ppb over a specified time period, usually during daylight hours (Figure 8.1). The index sometimes is referred to as the SUM06, which is identical to the SUM60 index except that units of ppm are used. The sigmoidal index is an exposure parameter that uses continuous concentration weighting between 0 and 1. Therefore, all concentrations are (nominally) included in the index, but they are weighted differently (with higher concentrations weighted more heavily that lower concentrations). Lee et al. (1988) noted that the sigmoidal type of concentration-weighted cumulative index did not involve the selection of an arbitrary discrete threshold concentration (as opposed to the selection of 60 ppb in the SUM60 index) which, from a biological perspective, could vary from species to species and from one stage of development to another.

Figure 8.1: SUM60 - A Cumulative Exposure Index



More recently, Lefohn (1994) has summarized some of the different types of indices that have been evaluated (but not including the sigmoidal indices) (Table 8.6).

Table 8.6 Summary of some ozone exposure-plant response indices

Index type	Index description
One event	The second highest daily maximum 1-h concentration (HDM2)
	The maximum of 7-h (P7) and 1-h (P1) maximum daily averages
	90th (PER90), 95th (PER95) and 99th (PER99) percentiles of hourly distribution
Mean	The seasonal mean of 7-h daily means (M7)
	The seasonal mean of 1-h daily peaks (M1)
	The effect mean (EFFMEAN) (Larsen and Heck, 1984)
Cumulative	The seasonal sum of hourly concentrations (TOTDOSE) or (SUM00)
	The seasonal sum of hourly concentrations at or above 0.06 ppm (SUM06), 0.07 ppm (SUM07), 0.08 ppm (SUM08), 0.10 ppm (SUM10)
	sum of hourly (08:00-19:59) concentrations at or above 60 ppb (SUM60)
	The seasonal censored sum of hourly concentrations at or above 0.08 ppm (AOT08) or 0.010 ppm (AOT10
	censored sum of hourly (07:00-21:00)concentrations at or above 40 ppb (AOT40)
	The total impact (TIMPACT) (Larsen et al., 1983)
	The ALLOMETRIC, in which the hourly concentration was weighted by raising to a power and summed (see Lee et al., 1989; Lefohn et al., 1988)
	Total hours with concentrations at or above 0.08 ppm (HRS08), or 0.10 ppm HRS10)
	The number of episodes (defined as an event with hourly concentrations above a threshold level) above a threshold of 0.08 ppm (NUMEP08), or 0.10 ppm (NUMEP10)
	The average episode length with threshold 0.08 ppm (AVGEP08), or 0.10 ppm (AVGEP10)
Multicomponent	Indices that incorporate several characteristics of exposure, including the phenologically weighted cumulative impact indices (PWCI) (Lee et al., 1987)

It is important to note that, in general, the relative performance of a given index/indices depends on the crop species, the experimental approach and data sets used. Lee et al. (1988), Lefohn et al. (1988), and Musselman et al. (1988) concluded that no single ozone exposure index performed equally well every time. Nevertheless, based on the relative performances of various indices, Lefohn et al. (1988, 1989) concluded that cumulative exposure indices could be used to describe ozone exposures for predicting agricultural crop effects. The findings by Lee et al. (1988) and Lefohn et al. (1989) stressed the importance of using cumulative indices instead of seasonal mean indices. In this regard, Larsen and Heck (1984) and, later, Hogsett et al. (1985b) demonstrated that it was possible for two sites with similar seasonal mean values to have different estimated crop impacts. In the latter study, greater impacts were demonstrated at a site with a lower seasonal mean using fluctuating episodic exposures compared with growth reductions at a similar site with a higher seasonal mean generated via lower, more repetitive daily exposures. Because some of the earlier NCLAN study results were published using the seasonal mean index, an exposure index that does not weight the higher hourly average concentrations, it has been difficult to use some of the results previously published. However, re-analysis of the NCLAN data, using alternative cumulative exposure indices, has allowed investigators to evaluate exposure-response relationships.

Additional insight concerning the possible problems associated with using a seasonal mean can be found in works published by Manning and Krupa (1992) and Legge and Krupa (1990). In general, the frequency distributions of hourly average concentrations (all 24 hours included) of ambient ozone exposure profiles do not exhibit a normal distribution. Rather, the frequency distribution of hourly ambient ozone concentrations is best described by the numerical functions of the Weibull family (Lefohn & Benedict, 1982; Legge & Krupa, 1990). In these distributions, there is a frequency peak to the left at low ozone concentrations, with a tail to the right towards high concentrations. The computation of arithmetic means with such non-normally distributed data is statistically inappropriate and can lead to artifacts in modelling ozone exposure- and crop-response relationships (Krupa & Kickert, 1987b). To the contrary, use of the geometric mean or the median value is free of the influence of this non-normal type of frequency distribution of the data. This approach, however, has not gained widespread acceptance and has been only occasionally referenced as a potential modelling approach for ozone exposure- and crop-response (Larsen & Heck, 1976). In spite of its suitability to non-normally distributed data, it too suffers from the drawback that it condenses the exposure variability in a single value.

With the trend towards a cumulative type expression of ozone exposure as a more biologically relevant methodology, several studies (Lefohn & Benkovitz, 1990; Pedersen & Lefohn, 1994; Lefohn & Foley, 1992) have attempted 'real world' application of these experimentally derived exposure indices to determine if they adequately capture the important features of ambient ozone exposure and vegetation impact. These studies have demonstrated the weaknesses of an averaging approach to exposure and have also pointed out limitations in a cumulative index approach, in that this method may require additional consideration of the frequency of high concentrations (Lefohn et al., 1992). For example, over a 100-day growing season, it is possible for two sites to end up with the same SUM60 value but have quite different frequency and intensity profiles of hourly ozone levels. One site could have a few episodic conditions resulting in very high levels over short periods of time and levels below 60 ppb for the remainder of the season. The other could have a larger number of days when ozone levels only marginally exceeded 60 ppb and few or no days when the hourly levels were high. The mathematics of the SUM60 for these two sites could yield a similar SUM60 value but, obviously, the frequency and intensity of the ozone profile could be dramatically different, resulting in a different biological impact.

Contrary to the previous conclusions that the higher hourly average concentrations should be provided greater weight than the mid- and low-level values, several papers have appeared recently in the literature that concluded that the mid-level ozone concentrations contribute more to vegetation effects than the higher values. Krupa et al. (1994) concluded that:

- hourly average ozone concentrations between 0.05 and 0.087 ppm (i.e., mid-range concentrations) may be the most important contributors to crop losses; and
- hourly average concentrations above 0.087 ppm may not be as important in predicting yield loss.

To arrive at these conclusions, the authors selected several data sets from the NCLAN sites at which: yield for plants in non-filtered chambers was the same as yield in ambient air plots; and plant yield in non-filtered chambers was less than plant yield in carbon filtered chambers. An approach was used whereby the cumulative frequency distribution (CFD) of cases with statistically significant negative yield effects (CF>NF) were combined and compared with selected no yield effect studies (CF=NF). The CFD is defined as follows:

$$\text{CFD50–87} = \text{Total \# Hours of Ozone} \geq 50 \text{ and} \leq 87 \text{ ppb} \div (\text{Total \# of Hours of Ozone} \geq 50 \text{ ppb})$$

The CFD approach utilized ozone data for a 24-hour period over the days of the growing season in which the individual NCLAN experiments were operational.

In a study in Germany, Grünhage et al. (1993) and Grünhage and Jäger (1994) reported that mid-range levels of ozone might be more important than high levels in response of plants to ozone exposure. In the 1993 study, Bel-W3 tobacco was used to examine the relationship between ozone flux and plant injury. The results from this study, which pointed to the importance of mid-range levels of ozone in the development of ozone injury, using this highly sensitive ozone-indicator plant, were similar to the earlier findings of Tonneijck and Bugter (1991). In the Grünhage and Jäger study, it was concluded that the conductivity of ozone into plants was normally low during the times of the day when ozone levels were high.

Legge et al. (1995) report that their results using both NCLAN and the European Open-Top Chamber Programme (EOTCP) data show that the cumulative frequency of occurrence of intermediate or moderate hourly ozone concentrations is important in crop yield-loss response. However, unlike their NCLAN findings, which showed that the cumulative frequency distribution (CFD) of hourly ozone concentrations between 0.050 and 0.087 ppm was the best predictor of crop response in the U.S., the corresponding results (using a modified statistical format due to EOTCP design differences) from the EOTCP showed a range of 0.035-0.060 ppm as being important in Europe. While it is concluded that these results demonstrate the importance of moderate hourly concentrations in inducing adverse crop-yield response, the authors underscore the fact that these conclusions do not negate the importance of peak hourly ozone concentrations, if such levels occur during periods when both optimal atmospheric and plant conductivities coincide.

As result of the papers published positing that mid-range concentrations are of greater importance than high values, a debate in the scientific community has arisen. In summary, the underlying reasons for the debate appear to stem from the use of atmospheric ozone concentrations as a surrogate for plant ozone dose. The findings from these studies have been subject to critical review by scientists who feel that the mid-range argument does not adequately describe plant response to season-long ozone exposure. Musselman et al. (1994) conclude that although these studies "all show a response of ozone sensitive plants to moderate concentrations of ozone, they do not provide conclusive data that sensitive plants are not responsive to higher ozone concentrations. Nor do they provide data that other less-sensitive plant species are more responsive to moderate concentrations than to high concentrations of ozone."

Legge et al. (1995) state that they have not concluded that high concentrations are less phytotoxic than mid-range concentrations; rather, they reason that because high concentrations tend to occur at times when ozone uptake by plants is lower, the actual dose absorbed by vegetation during periods of high ozone concentrations tends to be lower than the dose absorbed during periods of the day when plants experience mid-range concentrations. A summary of the response by Legge et al. (1995) is presented in Table 8.7.

In view of the debate that had emerged in the scientific literature and at conferences and meetings regarding the role of mid-range concentrations in ozone exposure–plant response relationships, (Krupa et al., 1994) and in consideration of scientific concerns raised regarding some of the statistical techniques that had been used in the NCLAN and EOTCP reanalysis (Krupa et al., 1994: Legge et al, 1995), the Vegetation Objective Working Group (VOWG) of the NO_x/VOC Science Program decided to more thoroughly evaluate the CFD exposure–response assessments that had been undertaken and described by Krupa et al. (1994) and Legge et al. (1995). The VOWG's re-analysis was conducted by utilizing all the NCLAN data (negative, positive and no-effect cases) identified by Krupa et al. (1994) and Legge et al. (1995). The analysis of this work was also undertaken to compare the effectiveness of the cumulative frequency based index used by Krupa et al. (1994) (CFD50–87), which focused only on the hourly average concentrations between 50 and 87 ppb, versus concentration-weighted cumulative exposure indices, which utilize a threshold value and place greater emphasis on higher ozone concentrations (i.e. SUM60 and AOT40).

Table 8.7 Summary of main arguments from Legge et al. (1995)	
Argument	**Supporting studies cited**
Ozone exposure conditions in open-top chambers do not reflect ambient exposure	Tonneijck and Bugter (1991) found a tendency for a reduced sensitivity of tobacco (Bel-W3) plants to relatively high ozone concentrations in the Netherlands Krupa et al. (1993) found that sums of all hourly concentrations > 0.040 ppm (SUM04) and > 0.06 ppm (SUM06) jointly proved to be the best predictors of median value of foliar injury on tobacco (Bel-W3) at two geographic locations in NE USA. Sum of all hourly concentrations > 0.07 or 0.08 ppm were not as important in explaining the cause-effect relationship. Grünhage and Jäger (1994) demonstrated that a combination of measured and modelled frequency distributions of differing percentages of leaf area injured on tobacco (Bel-W3) at various ambient concentrations of ozone, converted to their corresponding flux densities, showed that concentrations between 0.05 and 0.09 ppm are likely to have the most effect and may be more important than those > 0.09 ppm.
Ozone uptake and/or foliar injury or yield reduction due to ozone are highest at times when or where the ambient ozone concentrations are moderate	Grünhage et al. (1994) and Schmitt et al. (1995) reported that above two grassland ecosystems, the diurnal pattern of ozone deposition velocities reached peak values before noon, whereas the diurnal pattern of ozone concentrations attained peak values during the afternoon. Grulke (cited by Skelly, 1995) showed that trees of giant sequoia responded to low (ambient) values of ozone, not just high values. Showman (1991) reported that ozone injury to sensitive species was widespread in a moist year with low ozone levels, whereas injury in a dry year with high ozone concentrations was rare. Wieser and Havranek (1993) indicated that the diurnal pattern of ozone flux densities from the air to the needles of Norway spruce peak in the late morning, whereas the diurnal pattern of ozone concentrations peak in the afternoon. Wieser and Havranek (1995) reported that when ambient ozone concentrations were highest, ozone flux to the needles of European larch tended to be restricted by narrowing of the stomatal opening. Ojanperä et al. (1994) observed in OTC experiments that a 40-ppb threshold did not provide a significant correlation with changes in the grain yield of spring wheat, while the inclusion of all ozone concs. below 40 ppb provided an R^2 of 0.93.

Upon reviewing the methodology utilized in the Krupa et al. (1994) and Legge et al. (1995) studies, VOWG members questioned the conclusions that were drawn by the investigators. Concerns were associated with the use of the NCLAN data, the statistical approaches used in the analyses, and the accuracy of the regression analyses.

For its review, the VOWG used two approaches. The first was to focus on the use of the NCLAN data. When all the NCLAN data sets identified for the analysis (i.e., all cases of increased, decreased and no-yield effect between the carbon-filtered and unfiltered treatments where yield in unfiltered chambers was not statistically different than yield in ambient air plots) were pooled, cumulative indices (i.e., SUM06 and AOT40) were more closely correlated with plant responses to ozone than the truncated CFD50-87 index, which focused on the mid-range concentrations. In addition, the VOWG concluded that the inaccurate use of some of the NCLAN data identified cast uncertainty on the strength of the frequency-based CFD of mid-range concentrations as an air quality indicator of long-term (seasonal) adverse effects of ozone on crop yield.

The second approach utilized actual ozone hourly values from Canadian monitoring sites. The truncated CFD50–87 values (mean, maximum and minimum) for the 32 sites in Canada that can be classified as being representative of rural or forested areas were calculated. The truncated CFD50–87 technique provided a poor fit with areas of Canada with documented ozone effects on vegetation. In high ozone impact areas of southwestern Ontario like Simcoe, Long Point, Parkhill, Merlin, Tiverton and Huron Park, where foliar injuries and crop loss effects are well documented, the lowest CFD50–87 values were recorded (range of 0.8805–0.9446). In contrast, the highest possible CFD50–87 values (1.0) were recorded in remote northern areas of Ontario (Experimental Lakes Area), where crop effects have not been documented. This was also the case in areas like Cormack, Newfoundland, and Vegreville, Alberta. In other words, as the CFD50-87 increased, fewer exceedances of 82 ppb were recorded (r = -0.92).

As indicated previously, Legge et al. (1995) emphasized that their work pointed to the importance of mid-range concentrations, but acknowledged that if high concentrations occurred during the times of the day when plants are most sensitive, then they too would be considered important. However, given the manner in which the truncated CFD50–87 is calculated as proposed by Krupa et al. (1994), the VOWG concluded that, under ambient air quality conditions, this type of statement was difficult to rationalize. The occurrence of peak concentrations (values in excess of 87 ppb), defacto reduces the magnitude of the CFD50-87 index proposed by Krupa et al. (1994). The VOWG concluded that, based on the truncated CFD calculation methods, it is difficult to assert the importance of mid-range ozone concentrations of 50–87 ppb, while at the same time acknowledging that peak concentrations may also be important.

Although the scientific debate continues concerning the importance of mid-range versus high concentrations, the VOWG concluded that at present there was little support for the truncated CFD approach. This conclusion was based on the following:

- When all the NCLAN data sets identified for the analysis (i.e., all cases of increased, decreased and no-yield effect between the carbon-filtered and unfiltered treatments where yield in unfiltered chambers was not statistically different than yield in ambient air plots) were pooled, the two, cumulative indices (SUM06 and AOT40) were more closely correlated with plant responses to ozone than the CFD of the mid-range concentrations (CFD50-87).
- Inaccurate use of some of the NCLAN data was identified; in addition to the foregoing comparative analysis, this cast uncertainty on the strength of the frequency-based CFD of mid-range concentrations as an air quality indicator of long-term (seasonal) adverse effects of ozone on crop yield.
- The truncated CFD50–87 technique provided a poor fit with areas of Canada with documented ozone effects on vegetation

Based on the above reasons, the VOWG made the decision to focus on cumulative exposure indices.

Alternative cumulative exposure indices

The discussion that follows is a summary of the analysis undertaken by the Vegetation Objective Working Group of alternative forms of cumulative exposure indices. For the purposes of this discussion, the U.S. approaches are cited in their native form, i.e., in units of ppm; whereas the Canadian equivalents are cited in units of ppb. Crop yield response to ozone is inferred from a large collection of studies; in order for the results of different studies to be pooled together, the ozone exposures received by the plants must be normalized into a common expression that is a substitute for "dose". The NCLAN data for crop loss have used SUM06 (SUM60) to describe the exposure; many studies since that time have also described exposures in terms of SUM60. Much of the European work has used AOT40 to describe experimental exposures of ozone to plants. Other than these two data bases, there is a vast array of studies, both of acute and chronic exposures, for which neither AOT40 nor SUM60 were or can be calculated. This is because the air quality throughout the study was not monitored in a manner consistent with the calculation of these indices, and the studies are extremely difficult to harmonize with each other, and with the NCLAN data set. So, the choice of SUM60 as a candidate exposure index for evaluating plant response to ozone is supportable from the perspective of being able to evaluate the largest, normalized data base available.

However, because the hourly ozone data for the NCLAN studies were available, it was possible to test other indices of ozone exposure for description of the NCLAN crop yield data. For reasons described in the previous section, the truncated CFD approach was ruled out as a viable option. On the basis of published scientific studies and discussions within the U.S. on the need for an ecologically based secondary ozone standard, it was concluded that the most appropriate form of a vegetation-based air quality index was one that was cumulative in nature, with greater emphasis on peak versus mid-range concentrations and some type of phenological weighting. However, given the lack of phenologically linked dose response information required to develop a phenologically weighted index (this would necessitate a crop-by-crop, tree-by-tree and region-by-region approach), the decision was then focused on threshold-based cumulative indices. The weighting of an index based on sigmoidal curves reflective of potential flux factors (e.g., the W126 index) was also explored briefly, but was ruled out primarily for the reason that it was believed that from a regulatory aspect, this type of index would be complex and difficult to administer.

Consequently, the options for form of an ozone exposure index were reduced to SUM60 and AOT40 forms, both of which express ozone levels as ppb-h. The sections that follow describe how the final decision to adopt a SUM60 index was reached. Although both AOT40 and SUM60 are cumulative in the manner in which they sum ozone exposure values, there are three key differences:

1. The AOT40, by definition, takes ozone levels above 40 ppb into consideration, whereas the SUM60 does not start accumulating the hourly exposure to ozone until the concentrations reach 60 ppb (0.06 ppm).
2. The AOT values are censored by subtracting 40 from all hourly values > 40 ppb (i.e., a reading of 65 contributes 25 to summation process), whereas in the case of the SUM60 the entire value is used in the summation process for concentrations ≥ 60 ppb.
3. The AOT40 and SUM60 indices utilize hourly ozone values from different periods of the day; the AOT40 captures all ozone concentrations during the time of the day when global clear-sky radiation is above 50 W/m^2 during three months (normally May-July). If solar radiation information is not available, the hours from 07:00-21:00 are reported as defaults. In the case of the SUM60, the hourly 'window' is a 12-h period (08:00-19:59) using a running, three-month calculation process (for a seasonal SUM60 that is).

The AOT40 and SUM60 indices were evaluated by looking in more detail at a subset of the NCLAN data for which signficant chamber effects could be ruled out (i.e.: for NF = AA as presented in Table 8.8 (only SUM60 results shown). In this subset, exposure / plant response information is limited to a comparison of the charcoal filtered chambers (CF) and the ambient air plots (AA).

From the analysis of this subset (n=22) it was determined that:

1. The best performing indices were the SUM60 (12-h) and the AOT40 (12- and 15-h).
2. Modifying the AOT40 index to censor the data from 60 ppb instead of 40 ppb (effectively making it AOT60) and shortening the daylight period to 08:00 to 19:59 to match the SUM60 format, failed to improve the predictive capability of the AOT index.
3. The cumulative expressions of ozone exposure performed considerably better than the frequency of exceedance of the existing Canadian air quality objective of 82 ppb in predicting yield reductions.

Table 8.8: SUM60 values and Crop yield in a subset of NCLAN data where NF = AA*

Location	Year	Crop	SUM60 Adj.3 Mo. (08:00-19:59)	AA Yield	NF Yield	CF Yield	Yield Ratio NF/CF	Yield Ratio AA/CF
ARGONNE	1981	Maize	14,117	24.2	25.5	25.8	0.990	0.940
	1985	Soybean	18,337	14.9	14.4	14.9	0.966	0.999
	1983	Wheat	17,949	462.0	450.9	412.9	1.092	1.119
	1993	Soybean	23,736	15.4	16.1	17.1	0.940	0.899
Ithaca, N.Y.	1983	Wheat	29,011	33.8	34.4	44.6	0.770	0.757
	1982	Wheat	9,513	70.8	62.1	98.9	0.628	0.716
	1982	Kidney Bean	6,842	1,187.3	1,213.3	987.2	1.229	1.203
	1981	Soybean	990	16.2	15.6	16.3	0.957	0.994
	1980	Kidney Bean	5,073	1,349.4	1,374.9	1,660.2	0.828	0.813
	1984	Clover -Harv.1	12,562	132.3	98.8	52.6	1.876	2.515
	1984	Clover -Harv.2	5,628	39.5	48.4	37.1	1.305	1.066
	1985	Clover -Harv.1	10,279	68.5	23.2	55.5	0.419	1.236
	1985	Clover -Harv.2	7,634	11.0	6.9	13.6	0.507	0.813
Beltsville	1983	Soybean	39,212	17.7	18.2	19.5	0.933	0.908
Raleigh	1984	Clover -Harv.1	19,058	31.6	30.6	36.8	0.831	0.858
	1984	Clover -Harv.2	42,512	32.3	32.1	35.0	0.916	0.924
	1984	Clover -Harv.3	46,165	26.7	30.2	33.9	0.888	0.787
	1984	Clover -Harv.4	16,588	21.9	20.0	20.8	0.958	1.050
	1985	Clover -Harv.1	40,851	14.3	14.1	24.1	0.584	0.592
	1985	Clover -Harv.5	22,917	3.5	0.8	8.2	0.100	0.431
	1984	Soybean	19,422	16.7	16.5	17.7	0.930	0.939
	1983	Soybean	40,754	15.7	16.1	17.3	0.929	0.909

* Adapted from Table 6.3.1 in Report of the Vegetation Working Group (Multistakeholder NO_x/VOC Science Program, 1997)

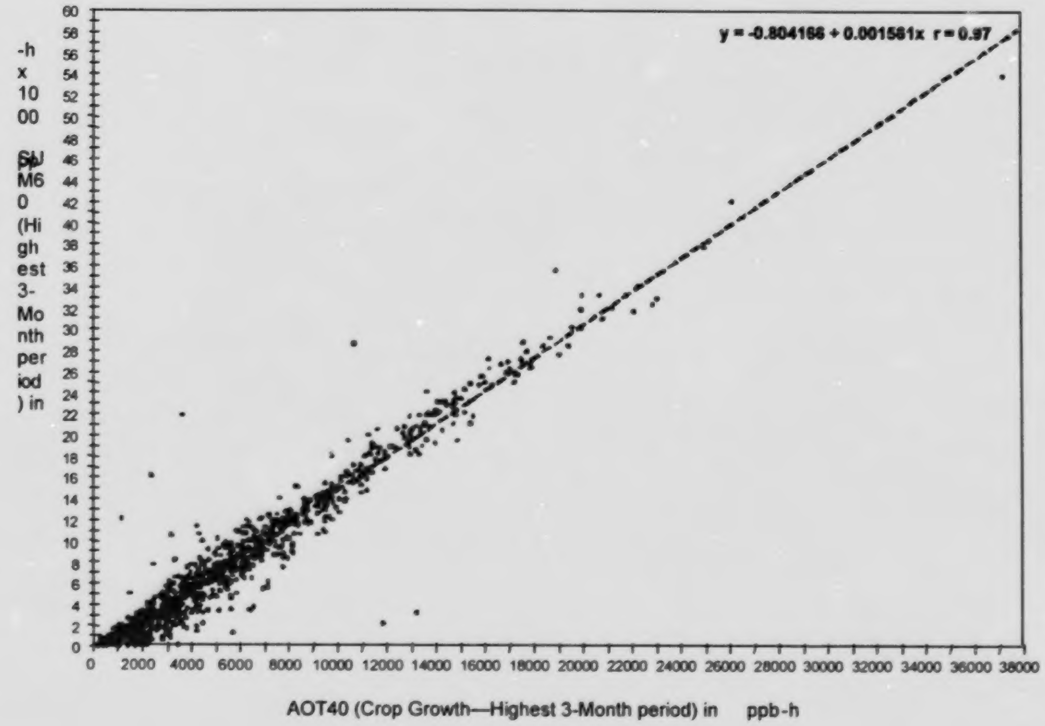
As a final step in the decision to recommend the SUM60 in preference to the AOT40 index, the Canadian air quality data for the period 1980-93 were assessed to explore the relationship between these two possible forms. A regression of these two indices is shown in Figure 8.2, and confirms a high degree of similarity ($r^2 = 0.97$). Therefore, it is concluded that, from an air quality management perspective, the decision to adopt a SUM60 index as opposed to an AOT40 makes little practical difference in terms of assessing the areas of ozone impact on Canadian vegetation.

Given the agreement of the two indices in predicting crop yield response and the high correlation between the two forms when looking at the ambient data, there appears to be no compelling scientific reason to select one over the other. Therefore, other factors were considered, including:

- support for the AOT40 resides primarily in Europe, where experimental studies via the EOTCP have concentrated mainly on three crops (spring wheat, green bean and pasture); although additional crops and trees are now being evaluated, the AOT40 Critical Levels for crops are still restricted to one agricultural species (wheat);
- support for the SUM60 resides primarily in the U.S., where the NCLAN program has provided exposure/response data for 15 crop species (corn, soybean, wheat, alfalfa, clover, fescue, tobacco, sorghum, cotton, barley, peanut, potato, lettuce, turnip and dry bean);
- although there may be greater similarity in climate between the major ozone impacted regions of Canada and some of those in Europe, where the EOTCP studies were conducted, than would be the case for some of the U.S. NCLAN sites, there was consensus that other factors (levels of other atmospheric contaminants, differences in the genetic composition of plants under study) in the European setting may be important and would favour the selection of the SUM60 over the AOT40; and
- given the geographical location of Canada relative to the U.S., and the importance of a coordinated approach to the resolution of air quality issues of such regional and transboundary nature, it was concluded that the harmonization of an air quality index to protect vegetation in both countries could lead to improved efforts in emission reduction strategies.

Based on the factors described above, a decision was reached by the VOWG to recommend the use of SUM60 as an index for describing ozone exposure-vegetation response relationships. This decision is supported by the Working Group on Air Quality Objectives and Guideines. However, it is noted that although the SUM60 clearly encapsulates some aspects of plant exposure that are important in the response (i.e. cumulative exposure over a time period and the relative importance of peak concentrations), there are other factors influencing the exposure-response relationship that are not accounted for in the SUM60 index (e.g. phenology, time of day). In the future, it may be possible to develop a more biologically relevant index.

Figure 8.2: Relationship Between SUM60 and AOT40—All Canadian Monitoring Sites (1980–1993)



8.2.3 Exposure-Response Relationships for Chronic Effects

Growth Reduction to Agricultural Crops

One of the most critical decisions that must be made in any assessment of season-long yield reduction is to establish the limits of experimental certainty with respect to final yield or biomass loss. Based on recent analyses undertaken in Europe (Fuhrer, 1994) and the U.S. as part of their Critical Level and Secondary Standard development processes, respectively, the lowest possible precision from experimental, season-long ozone exposures involving crops has been estimated at from 5-10% (i.e., loss estimates below 5-10% would be within the range of experimental error). Given the additional variability and uncertainty regarding the application of the experimental findings from open-top chambers to real-world field conditions, a yield loss minimum value of 10% is utilized in this assessment. It is recognized that a 10% yield-level decision could, under many agricultural situations, represent virtually all of the economic profit margin for a typical crop producer. However, given the uncertainty that currently exists in the available experimental findings it has been concluded that this is the best that can be achieved at this time.

Another factor that must be considered in the process of trying to define an ambient ozone level above which effects on Canadian vegetation occur, is that the research cannot possibly cover all crops/cultivars, trees or species of native vegetation growing in a country the size of Canada. The recommendation of an 'effects-level' will arise from a data base which contains information on perhaps half of the 'important' agricultural and woody tree species, and virtually no native herbaceous species.

The NCLAN experimental protocol was designed to produce crop exposure-response data (See Box 1). In the U.S. EPA review of the NCLAN data to support discussion on the form and level of a secondary standard for ozone, a subset of the NCLAN data was identified as being most appropriate for this type of evaluation (U.S. EPA, 1996). In order to use these data to develop LOAELs in a Canadian context, a further subset was created by removing those crops not grown in Canada as well as those evaluated under Californian growing conditions. This set of crops, with 3 month, 12-h SUM60 values corresponding to 10% yield loss levels are shown in Table 8.9 (n = 42). The 10% yield loss levels were calculated from individual regression analyses of yield data from all NCLAN studies on a particlar crop (U.S. EPA, 1996). There is insufficient information in this subset to identify NOAELs.

Box 1: NCLAN Protocol[1]

The U.S. National Crop Loss Assessment Network (NCLAN) Program was set up in 1980 to provide the data needed to assess the economic consequences of air pollution on major agricultural crops. This called for experiments to be conducted to better the relationships between crop yield and different doses of O_3, SO_2 and NO_2, individually and in combination. Initially, the focus of NCLAN was on O_3 because this information was required as part of the review in the U.S. of the secondary National Ambient Air Quality Standard (NAAQS) for ozone.

Six field sites in the NE, SE (2), Central, SW and NW of the United States were established to study ozone exposure - crop yield relationships for a number of important crops. The experimental protocol was designed explicitly to minimize differences in growing conditions, to use realistic pollutant concentrations and to allow analysis of the data by both ANOVA and regression techniques. OTCs (3 m diameter) and standardized ozone dispensing and monitoring systems were utilized. Each experiment consisted of a series of 4-6 ozone treatments replicated 4 times in a randomized block design for a total of 24 plots per site per crop cultivar.

The standard treatments were as follows:

AA	Ambient air plot, no chamber.
CF	OTC plot, charcoal filtered air. Control plot, where ozone concentration was approximately 25 ppb, intended to represent natural background ozone.
NF1	OTC plot, non-filtered air. Ozone concentration approx. equal to ambient air.
NF2	NF1 plus an additional 30 ppb ozone.
NF3	NF1 plus an additional 60 ppb ozone.
NF4	NF1 plus an additional 90 ppb ozone.

For NF treatments, ozone was added for 7 hours per day between the hours of 0900 and 1600 (Standard Time). Ozone concentrations within the plots were monitored at canopy height, for 2-3 minutes about 2-3 times per hour. The NCLAN adopted a seasonal 7 hr/day mean O_3 concentration as its index of plant exposure. The 0900 - 1600 time period was selected to include the hours of the day when plants are most active and when ozone concentrations are generally highest. The "season", as defined by the NCLAN protocol, covered only the period of time during which O_3 treatments were administered, and therefore varied with each crop.

Plants were harvested from all plots when CF plants reached maturity. Based on the protocol, comparisons of NF1 plot yields with AA plot yields were used to test for chamber effects. Plot yields were reported as both absolute yields and as a percentage of predicted yield at the control concentration (CF plot, O_3 concentration approx. 25 ppb). Dose-response relationships were first developed for individual crop cultivars. Then, where possible (i.e. where homogeneity across the individual responses existed), combined dose-response functions were calculated as the simple average of individual loss functions. A number of linear and non-linear dose-response functions have been developed and evaluated using the NCLAN data.

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[1] The information in this Box was compiled from the following sources: Heck et al., 1982; Heck et al., 1983; Heck et al., 1984). The original papers should be referred to for further detail on methodological aspects of the NCLAN Program, particularly regarding the objective of developing better physiological models of plant response to air pollution, a subject not covered in this Box.

Table 8.9 Summary of NCLAN SUM60 index values resulting in a 10% yield loss in NCLAN studies.

Crop Evaluated[1]	Cultivar	Moisture Status	12-hour SUM60 (ppb-h)
Corn (L)[2]	PIO		41,600
	PAG		55,800
Kidney Bean	CAL LT RED		15,200
Kidney Bean (L)	CAL LT RED		17,200
Peanut (L)	NC-6		36,200
Potato	NORCHIP		9,900
	NORCHIP		20,300
Sorghum	DELALB		67,600
Soybean	CORSOY		15,300
	CORSOY		42,200
	AMSOY		32,800
	PELLA		18,200
	WILLIAMS		15,500
	CORSOY	Dry	71,200
	CORSOY	Wet	70,000
	CORSOY	Dry	89,100
	CORSOY	Wet	62,200
	CORSOY	Dry	10,200
	CORSOY	Wet	11,800
	WILLIANS	Dry	21,100
	WILLIAMS	Wet	14,800
	HODGSON		8,400
	DAVIS		13,800
	DAVIS		23,400
	DAVIS	Dry	57,100
	DAVIS	Wet	35,200
	DAVIS	Dry	45,900
	DAVIS	Wet	24,100
	YOUNG	Dry	38,800
	YOUNG	Wet	25,000
Tobacco (L)	MCNAIR		24,400
			cont.

Table 8.9 Summary of NCLAN SUM60 index values resulting in a 10% yield loss in NCLAN studies.

Crop Evaluated[1]	Cultivar	Moisture Status	12-hour SUM60 (ppb-h)
Turnip (T)	JUST RIGHT		7,400
	PURPLE TOP		5,900
	SHOGOIN		6,600
	TOKYO CROSS		9,300
Wheat	ABE		25,100
	ARTHUR		21,300
	ROLAND		7,400
	ABE		34,800
	ARTHUR		27,700
	VONA		2,900
	VONA		7,700

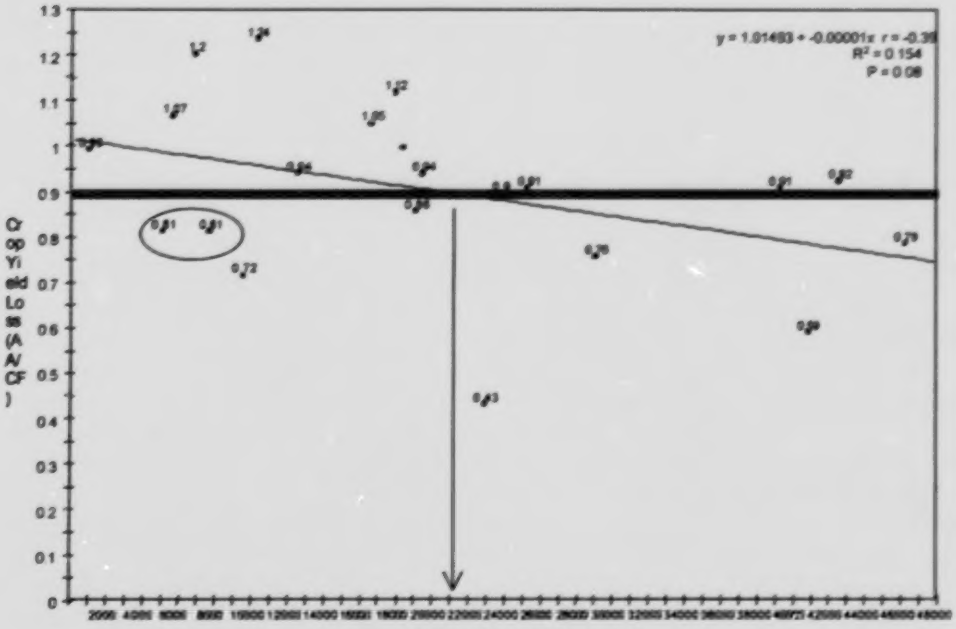
[1] excluding cotton and crops assessed in California.

[2] (L) log transformation used to stabalize the variance (T) yield expressed as g/plant. A weibull model was fit to all other studies, and all other yields are expressed in kg/Ha.

The lowest SUM60 value at the 10% yield loss level is 2,900 ppb-h for wheat cultivar VONA. The next most sensitive species were turnips and other wheat cultivars spanning the range 5,900 to 7,400 ppb-h. The SUM60 level corresponding to the median crop biomass loss at the 10% yield loss level is 38,000 ppb-h (U.S. EPA, 1996, Figure 5-23). At an expert workshop convened in January 1996 on the ozone secondary standard, there was consensus that a more conservative approach should be taken, namely that the ppb-h when 25 and 35% of the crops had 10% or more yield loss should be considered (Heck and Cowling, 1997). This corresponds to 15,000 and 20,000 ppb-h respectively.

To further the identification of a LOAEL, the data for which chamber effects were considered negligible (Table 8.8) were reviewed again (Legge et al. 1993). Figure 8.3 presents the regression analysis of these data (i.e. between crop yield loss and the 3-month SUM60). From the regression curve of Figure 8.3, the level at which 10% yield loss is predicted is about 21,000 ppb-h. The LOAELs observed from this analysis were 5,000 to 7,700 ppb-h, as indicated by the circled data points in Figure 8.3. At these SUM60 levels, the two crops in question experienced a 20% yield loss (approximately). Although the LOAELs from the two data sets (Table 8.9 and Figure 8.3) are for slightly different endpoints (10% vs. 20% yield loss), the similarity in the range of LOAELs lends some confidence to these levels. Similarly, the average 10% yield loss levels from the two data sets are also reasonably close (38,000 vs. 21,000 ppb-h).

Figure 8.3 Relationship between SUM60 and crop yield loss (AA/CF) for NCLAN data subset where NF=AA.



Note: SUM60 values for two crops (Argonne-1981-Maize and Raleigh-1983-Soybean) were selected from the 3-month period corresponding with reproductive growth. Ithaca 1984 clover Harvest 1 excluded as an outlier.

In terms of estimating plant response under conditions of enhanced ozone exposure it was reasoned that if the plant response to ozone was enhanced as a result of the use of experimentally elevated ozone treatments in the NCLAN studies, then the SUM60 values for 10% yield loss derived from the full treatment regression approach (listed in Table 8.10 which includes only crops from Table 8.9 that match those in Table 8.8) using all experimental additions of ozone should be out of line with the analysis of the NCLAN subset where NF = AA (Table 8.8). The average SUM60 value corresponding to a 10% yield loss level for the three crops in common (kidney bean, soybean and wheat) from Table 8.10 was 29,200 ppb-h. To compare, the average SUM60 value corresponding to a 10% yield loss level when no ozone was added to the chambers (Figure 8.3 and Table 8.8) was ~21,000 ppb-h These two estimates are quite close considering the uncertainties associated with using the NCLAN data for this type of analysis. If anything, it appears as if plant response under experimentally elevated ozone concentrations is less than under the ambient exposure conditions.

Table 8.10: Crop yield loss selected for comparison with ambient air exposure treatments from the Legge et al. NCLAN re-analysis.

Crop Evaluated	Cultivar	Moisture Status	12-hour SUM60 (ppb-h)
Kidney Bean	CAL LT RED		15,200
Kidney Bean (L)	CAL LT RED		17,200
Soybean	CORSOY		15,300
	CORSOY		42,000
	AMSOY		32,800
	PELLA		18,200
	WILLIAMS		15,500
	CORSOY	Dry	71,200
	CORSOY	Wet	70,000
	CORSOY	Dry	89,100
	CORSOY	Wet	62,200
	CORSOY	Dry	10,200
	CORSOY	Wet	11,800
	WILLIANS	Dry	21,100
	WILLIAMS	Wet	14,800
	HODGSON		8,400
	DAVIS		13,800
	DAVIS		23,400
	DAVIS	Dry	57,100
	DAVIS	Wet	35,200
	DAVIS	Dry	45,900
	DAVIS	Wet	24,100
	YOUNG	Dry	38,800
	YOUNG	Wet	25,000
Wheat	ABE		25,100
	ARTHUR		21,300
	ROLAND		7,400
	ABE		34,800
	ARTHUR		27,700
	VONA		2,900
	VONA		7,700
		Average	29,200

Obviously, this type of assessment is also subject to considerable experimental error (due mainly to the utilization of a small subset of the NCLAN data; however, based on conclusions reached by vegetation experts at the Southern Oxidant Study (SOS) Workshop in Raleigh, NC (Heck & Cowling, 1997) and by others involved in the two major ozone air quality standard development efforts in Europe and the U.S., and subject to all the normal caveats associated with the development of air quality criteria, there appears to be no compelling reason to discard the NCLAN studies based on these concerns. The earlier work in California using air quality gradients (Musselman et al., 1988) as well as the numerous studies documenting vegetation impacts via the use of chemical protectants also provides support for using the NCLAN dataset.

Therefore, the relative yield loss data from the crops which received experimentally elevated ozone concentrations appears equally valid to those for which chamber effects are considered negligible, for estimating LOAELs and average 10% yield loss levels. In fact it is probably better because it spans a broader range of ozone concentrations and includes more crops.

However, considering the limitations of the NCLAN experimental protocol and dataset for purposes of identifying LOAELs (Box 1), it was considered inappropriate to simply select the lowest SUM60 from Table 8.9. Based upon the grouping of wheat and turnip harvest yield reductions in Table 8.9, a more conservative estimate of the LOAEL for reduced yield due to ozone exposure is in the range of 5900 to 7400 ppb-h

Additional Support for SUM60 Form and LOAEL Estimates for Crop Yield Reductions

The selection of the recommended form (SUM60) and LOAEL estimate is further supported by a review of the the chemical protectant studies that had been undertaken in Ontario during the period 1976-81 (most under research contracts between the Ontario Ministry of Environment and Energy (MOEE) and the University of Guelph). This required a reanalysis of all ozone-monitoring data from sites located as close as possible to the research sites. In a few cases, the experimental sites were too far from monitoring sites for these to provide useful ozone exposure information. These sites were therefore discarded. For a discussion of the detailed analysis the reader is referred to the Report of the VOWG (Multistakeholder NO_x/VOC Science Program,1996).

Yield loss data for a total of four crops (white bean, potato, tomato and cucumber) were assessed relative to the SUM60 (June–August) and exceedances of the 82 ppb hourly objective during the same 3-month period. The conclusions drawn from this analysis are summarized below.

- In the case of the all-crop analysis, a marginally significant relationship was found between SUM60 and yield ratios; however, the variability was high and precluded any meaningful predictive analysis.
- In the case of white beans, the relationship was considerably improved. However, in all cases, exposures were at levels in excess of the estimated LOAEL range of 5,00 to 7,400

ppb-h. Thus, a conclusion regarding the effectiveness of a 3-month SUM60 in this range to provide protection to this crop cannot be drawn from these data.

- In all cases except tomato, the SUM60 index of air quality was measurably better than exceedances of an hourly level of 82 ppb in terms of its ability to predict crop yield loss.

Although the analysis of this historical research appears to signal a weak relationship between the SUM60 index and crop response, caution must be exercised in the interpretation of these data for several reasons.

- In almost every report summarizing the findings of this research, it was pointed out that the chemical protectant (EDU) was unable to provide complete foliar injury protection and, accordingly, the EDU treatment may not be an accurate measure of growth/yield potential under ozone-free conditions; similar conclusions regarding the interpretation of chemical protectant studies were reached by Heagle (1989).

- In almost every study, a high degree of cultivar variability was experienced in the response to EDU application; this negated any attempt to elucidate causal relationships; again, Heagle (1989) expressed similar concern regarding the effectiveness of this material as reflected in the wide variability in the reported research findings.

Given these factors, the only conclusion that can be drawn from these studies is that yield losses of greater than 10% were frequently observed at SUM60 values as low as 9,000-10,000 ppb-h. Given the ineffectiveness of the EDU applications in terms of foliar injury response, it is not unreasonable to conclude that yield reductions were probably occurring at levels well below these values.

Growth Reduction to Trees

In the late 1980s, the U.S. EPA developed a program to assess the impact of ozone on forest trees of the U.S. via an OTC exposure protocol similar to that of the NCLAN. The findings of that assessment have been summarized by Hogsett et al. (1995) and also in the most recent EPA Staff Paper (1996). The method used in this study for determining the impact of ozone on forest trees is fully described in Hogsett et al. (1997), although tree response data are not presented and most of the tree response data from which this analysis was derived are cited as personal communication. Because the data are not available for inspection, it is not possible to display the exposure-responses for the various species on one graph as was done for the crop yields. However, the regression relationships between the normalized exposure (SUM06) and relative loss of biomass for all the cultivars and harvests were presented in Hogsett et al. (1997) as a single pooled Weibull relationship connecting the 50th percentiles of the range of relative biomass losses at values of SUM06 ranging from 10 to 60 ppm-h (10,000 to 60,000 ppb-h). Because this calculation collapses all species and cultivars into one exposure-response relationship, the SUM60 value corresponding to a 10% loss of biomass in individual species has been extracted from an earlier presentation (Hogsett et al., 1995) and is presented in Table

8.11. The values range from 4.4 ppm-h (4,400 ppb-h) for black cherry to 250 ppm-h (250,000 ppb-h) for Douglas Fir and Red Alder.

Table 8.11: Exposure-response data for 10% level of biomass loss, for trees exposed in OTCs to ozone .

Tree Species Evaluated	12-hour SUM60 (ppb-h)
Aspen – wild	19,100 15,800 43,700 55,900 55,400 18,700
Aspen 216	14,700
Aspen 253	8,100
Aspen 259	4,700
Aspen 271	13,300
Aspen 216	9,500
Aspen 259	5,200
Aspen 271	29,600
Aspen – Wild	15,000
Douglas Fir	89,300 250,000 90,800 94,400 72,000 70,800 63,000
Ponderosa pine	17,900 26,300 18,500 27,100 11,300 21,600 19,500 14,900 27,900 55,200 cont.

Tree Species Evaluated	12-hour SUM60 (ppb-h)
	43,400.
Red Alder	32,100
	17,900
	79,000
	38,008
	250,000
	21,800
Black Cherry	6,600
	4,400
Red Maple	71,700
Tulip Poplar	23,400
	19,900
	14,700
Loblolly GADR 15-91	71,000
Loblolly GAKR 15-23	212,100
Sugar Maple	25,300
	23,800
E. White Pine	21,600
	31,500
Virginia Pine	191,200

Source: Hogsett et al. 1995

The table shows that the SUM60 LOAEL estimates at the 10% biomass loss level, range from 4,400 to 6,600 ppb-h, based upon the response of black cherry and aspen 259 tree species.

8.2.4 Form of an Exposure Index – Acute Effects

Given the importance of protecting plants from both acute and chronic foliar injuries which may negatively impact crop quality and marketability, the development of a short term exposure index was considered. This was underscored in a publication of Lefohn et al. (1992), who suggested that the seasonal, cumulative-index approach to assessing crop response to ozone exposure may require additional consideration of the frequency and episodicity of short-term, high concentrations (since these are not specifically accounted for in the utilization of a seasonally-based cumulative index), if plants are to be protected from short term injury also.

Because there was no systematic attempt within the NCLAN program to draw relationships between ozone exposure and foliar injury, and because the work which forms the basis for the European short-term AOT40s was difficult to translate into protection provided via a SUM60 index under Canadian growing conditions, data from ongoing investigations into foliar injury in

Ontario and from the database of air quality ozone monitoring at rural and forested sites across Canada were utilized.

The following key issues were addressed:

- Is it necessary to implement a short-term index of ozone air quality, or will a 3-month seasonal SUM60 accurately describe the relationship between exposure and acute acute injury as well?
- If necessary, what form of short-term index best describes the relationship between acute exposure and foliar injury development?

These questions were addressed first by examining foliar-injury development on two crops in Ontario where such injury had been documented and could be linked with ozone air quality.

Ontario Case Studies

Case 1: Radish

In 1994, the MOEE investigated a case of extensive damage to a crop of radish in the Hamilton area. The foliar symptoms were characteristic of ozone-induced injury and had affected two harvests. In the first harvest, injury was estimated at 11-35% of the leaf area, while in the second harvest (five days later), injury was less severe, ranging from 2 to 10%. These symptoms had a negative impact on the appearance and, ultimately, the marketability of the crop.

In an attempt to explore the relationship between the severity of the foliar symptoms and several potential short-term indices, and to contrast these indicators of ozone air quality with the three-month SUM60 and exceedances of the existing one-hour ozone objective of 82 ppb (designed to provide protection against foliar symptoms), the air quality data from three of the closest air quality monitoring stations in the vicinity of the farm were analyzed. The results are presented in Table 8.12. Based on this information, the following conclusions were drawn:

- severe foliar injury was documented at a site where the average three-month SUM60 level was under 6,700 ppb-h (within the LOAEL range presented in section 8.2.3);
- a SUM60 calculated from ambient ozone concentrations over a three- or five-day period during the previous 15 days (prior to injury appearance) was unable to differentiate the severity of injury between the two plantings (injury severity levels of 11-35% vs. 2-10%);
- a SUM60, calculated from ambient ozone concentrations over a one-day period, did differentiate between the injury experienced in the two plantings (one-day SUM60 of 918 vs. 750 ppb-h for 11-35% and 2-10%, respectively);

- the frequency of exceedance of the existing hourly ozone objective of 82 ppb during the previous 15 days was also related to the degree of foliar injury (12 vs. 5 hours of 82 ppb for 11-35% and 2-10%, respectively).

Table 8.12 Assessment of foliar injury to radish and ozone levels at monitoring sites near Hamilton, Ontario (1994)

Station No.	3-month basis (April-June)		Previous 15 days (prior to harvest)							
			Harvest #1 (May 17-June 2) 11-35% foliar injury				Harvest #2 (May 24-June 7) 2-10% foliar injury			
	SUM60 (ppb-h)	Total hours 82 ppb	Max. 1-day SUM60 (ppb-h)	Max. 3-day SUM60 (ppb-h)	Max. 5-day SUM60 (ppb-h)	No. hours 82 ppb	Max. 1-day SUM60 (ppb-h)	Max. 3-day SUM60 (ppb-h)	Max. 5-day SUM60 (ppb-h)	No. hours 82 ppb
29,105	5837	16	860	1,374	1,393	11	718	1,374	1,393	5
29,114	8396	21	884	1,675	1,675	13	816	1,675	1,764	6
29,118	5841	11	1,010	1,485	1,374	11	716	1,485	1,485	4
Average	6691	16	918	1,511	1,481	12	750	1,511	1,547	5

Therefore, the two forms that appeared to provide the best fit with the severity of the injury were the number of exceedances of the existing one-hour ozone objective (82 ppb) and a cumulative one-day SUM60.

Case 2: White Bean

In 1995, the MOEE undertook a more detailed evaluation of foliar injury to the white bean crop in southwestern Ontario (Emerson, 1996). Unlike the normal, ongoing assessment that has been undertaken since the late 1970s, the 1995 assessment included an evaluation of foliar injury on about 90 varietal plantings located at nine different sites. The plants were rated on the basis of an injury index (scale of 0-100) by inspection of each variety plot for foliar ozone damage (stippling/bronzing). A numerical injury rating (from 0 to 6) was assigned that represented the average severity of injury to the plot as shown below:

Rating	Criteria
0	No oxidant symptoms observed
1	Scattered stippling on a few of the oldest leaves
2	Scattered stippling over most of the leaves
3	Moderate stippling or bronzing over a few of the leaves
4	Moderate stippling or bronzing over most of the leaves with some coalescence into flecks
5	Severe stippling or bronzing coalescing into necrotic flecks on many of the leaves; some premature leaf senescence and initial defoliation
6	Severe stippling or bronzing and coalescence on almost all leaves; plants prematurely senescent and defoliation occurring

The seven injury rating levels fall into five general injury-severity categories: no injury (0), trace (rating 1), light (ratings 2-3), moderate (rating 4) and severe (ratings 5-6). In order to compare the overall severity of ozone bronzing/stippling on white beans between locations, an injury scoring method was devised such that the injury ratings could be reduced to a single numerical score for each location and year. The injury-index scores were derived by calculating the percentage (%) of observations in each injury category (relative to total number of observations), and then multiplying the percentage (decimal) values by weighting factors as follows:

Trace (x 5)

Light (x 25)

Moderate (x 50)

Severe (x 100)

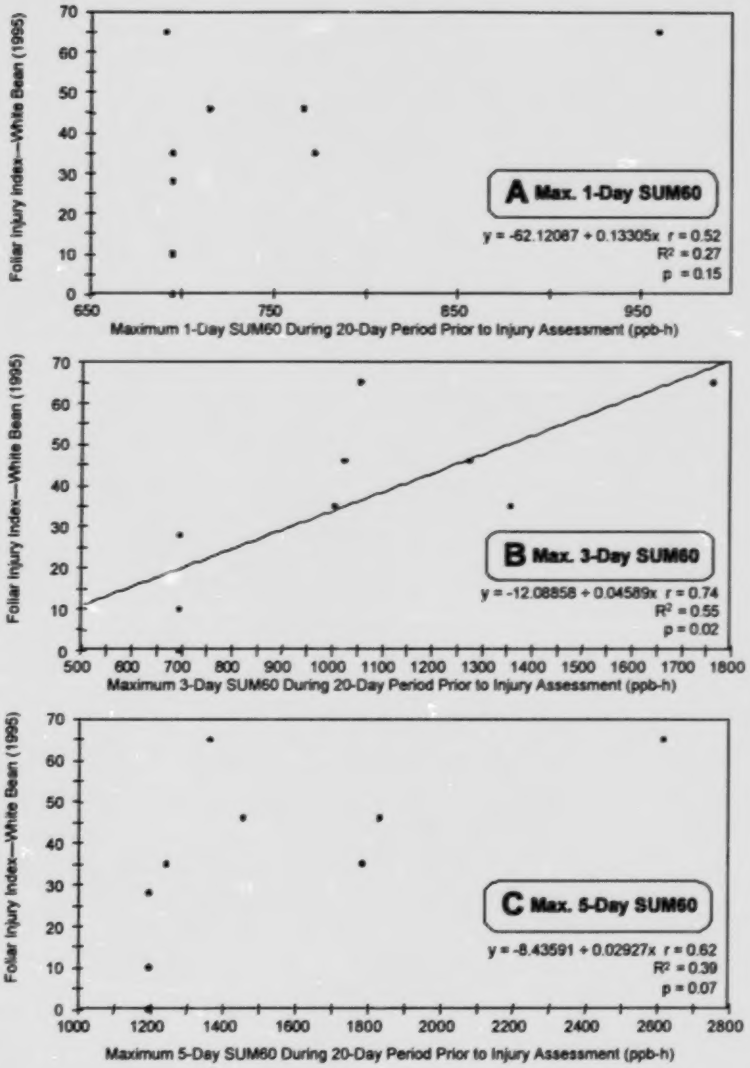
The total injury index score for each location/year was calculated by totaling the weighted scores for all injury categories. For example, if 30% of plots fell in trace category (0.3 x 5 = 1.5), 30% in light (0.3 x 25 = 7.5), 20% in moderate (0.2 x 50 = 10) and 20% in severe (0.2 x 100 = 20), the total injury index score was 1.5 + 7.5 + 10 + 20 = 39, out of a maximum 100. For purposes of interpretation, a score between 1-20 was classed as trace, between 21-35 as light and between 36-50 as moderate. A score of greater than 50 was classed as severe.

As for the radish injury assessment, the ozone air quality at nine sites (extrapolated from the closest rural monitoring stations in 1995) was assessed for a relationship with injury severity on white bean (Table 8.13). Statistical analyses were performed to explore the relationships between three potential short-term cumulative ozone indices (1-day, 3-day and 5-day SUM60), the existing 1-hour ozone objective (82 ppb) and the 3-month SUM60. Plots of the three short-term SUM60 indices and injury index severity are shown in Figure 8.4.

Table 8.13: Assessment of Potential Short Term Indices Based on Foliar Injury to White Bean in Ontario (1985)

Year	Crop Location	Previous 20-Day Period				June–August Period		Foliar
		Max. 1-day SUM60 (ppb-h)	Max. 3-day SUM60 (ppb-h)	Max. 5-day SUM60 (ppb-h)	No. hours = > 82 (ppb)	3-Month SUM60 (ppb-h)	No. hours = > 82 (ppb)	Injury Index (0–100)
1995	Elora	766	1275	1829	3	17911	44	46
1995	Harrow	959	1762	2615	20	28942	87	65
1995	Ridgetown	866	1559	2199	15	24735	72	35
1995	Huron Park	691	1055	1361	3	16630	48	65
1995	Brussels	718	1110	1460	6	16453	47	46
1995	Shetland	721	915	1391	7	17005	51	35
1995	Meaford	695	695	1195	5	15243	47	28
1995	Chesley	695	695	1195	5	15243	47	10
1995	Bervie	695	695	1195	5	15243	47	0

Figure 8.4 Foliar Injury to White Bean in Ontario and Short-Term SUM60s (1995)



The following conclusions were drawn from the 1995 white bean foliar injury-ozone air quality assessment (detailed statistical analyses are presented in the Report of the Vegetation Objective Working Group (Multistakeholder NO_x/VOC Science Program, 1997, VOWG):

- the three-month SUM60 (ppb-h) for the period June-August was unrelated to the severity of foliar injury ($p = 0.134$);
- the number of exceedances of the existing Canadian air quality objective for ozone during the three-month period of June-August was unrelated to the severity of foliar injury ($p = 0.244$);
- the number of exceedances of the existing air quality objective of 82 ppb during the previous 20 days (from the date of injury assessment) was unrelated to the severity of foliar injury ($p = 0.318$);
- of the three short-term cumulative SUM60 indices, the 3-day index performed the best ($p = 0.021$; this was followed by the 5-day and 1-day indices ($p = 0.072$ and 0.147, respectively.

Based on the foregoing analysis for 1995, a decision was made to reassess the foliar injury assessments of previous years, which, although not as extensive as in 1995, have been ongoing in southwestern Ontario over the past decade (1985-95). The data from this assessment are shown in Table 8.14, (details of the statistical analysis are presented in the Report of the Vegetation Objective Working Group (Multistakeholder NO_x/VOC Science Program, 1997, VOWG). Figure 8.5 (A-D) displays the relationship between the short-term cumulative indices (1- and 3-day SUM60s, scatter plots A and B) as well as with the maximum 1-hour ozone concentration (scatter plot C) and exceedances of the existing 1-hour ozone concentration of 82 ppb (scatter plot D) during the 20-day period preceding injury assessment in each of the 11 years. An analysis of the 5-day SUM60 is unfortunately not available.

Table 8.14 Assessment of potential short-term indices based on foliar injury to white bean in Ontario (1985-1995)

Year	Crop Location	Previous 20-Day Period												Foliar Injury Index
		Max. 1-day SUM60 (ppb-h)	No. of 1-day SUM60 = > 300 (days)	No. of 1-day SUM60 = > 400 (days)	No. of 1-day SUM60 = > 500 (days)	No. of 1-day SUM60 = > 700 (days)	Max. 3-day SUM60 (ppb-h)	No. of 3-day SUM60 = > 500 (days)	No. of 3-day SUM60 = > 700 (days)	No. of 3-day SUM60 = > 900 (days)	No. of 3-day SUM60 = > 1100 (days)	Max. 1-h (ppb)	No. Hrs =>82 (ppb)	(0-100)
1995	Elora	766	5	3	3	1	1275	10	5	3	2	83	3	46
1995	Harrow	959	8	7	6	3	1762	15	15	15	10	121	20	65
1995	Ridgetowr	772	5	4	4	2	1356	9	9	9	5	101	10	35
1995	Huron Park	691	4	2	1	0	1055	4	2	2	0	93	3	65
1995	Brussels	715	5	3	2	0	1024	7	3	3	2	100	6	46
1995	Shetland	695	2	2	1	1	1005	5	4	2	0	100	5	35
1995	Meaford	695	4	3	2	0	695	6	0	0	0	97	5	28
1995	Chesley	695	4	3	2	0	695	6	0	0	0	97	5	10
1995	Bervie	695	4	3	2	0	695	6	0	0	0	97	5	0
1994	Elora	762	4	4	4	1	2017	8	4	4	3	88	5	51
1994	Huron Park	675	4	4	3	0	1765	8	5	3	3	88	1	79
1993	Harrow	640	5	4	2	0	1294	8	8	2	1	83	1	40
1993	Ridgetowr	526	3	2	1	0	1072	5	4	2	1	77	0	54
1993	Huron Park	455	2	1	0	0	834	3	3	0	0	81	0	21
1992	Harrow	597	3	3	2	0	1269	6	3	2	1	79	0	72
1992	Huron Park	728	5	5	3	1	1812	7	4	4	4	90	6	15
1991	Harrow	778	6	3	1	1	1527	8	6	4	2	87	2	30
1991	Ridgetowr	778	6	3	1	1	1527	8	6	4	2	87	2	43
1991	Huron Park	799	8	6	5	2	1962	7	7	5	4	110	11	56
1990	Harrow	883	8	5	4	2	2065	11	10	6	5	104	13	88
1990	Ridgetowr	883	8	5	4	2	2065	11	10	6	5	104	13	75
1990	Huron Park	791	5	3	2	1	1453	10	5	4	3	85	5	68
1987	Ridgetowr	809	6	5	5	2	2215	10	6	5	5	116	8	48
1987*	Huron Park	827	4	4	4	4	2330	8	5	5	3	105	15	29

Table 8.14 (cont'd) Assessment of potential short-term indices based on foliar injury to white bean in Ontario (1985-1995)

Year	Crop Location	Previous 20-Day Period												Foliar Injury Index (0-100)
		Max. 1-day SUM60 (ppb-h)	No. of 1-day SUM60 = > 300 (days)	No. of 1-day SUM60 = > 400 (days)	No. of 1-day SUM60 = > 500 (days)	No. of 1-day SUM60 = > 700 (days)	Max. 3-day SUM60 (ppb-h)	No. of 3-day SUM60 = > 500 (days)	No. of 3-day SUM60 = > 700 (days)	No. of 3-day SUM60 = > 900 (days)	No. of 3-day SUM60 = > 1100 (days)	Max. 1-h (ppb)	No. Hrs =>82 (ppb)	
1987	Kippen	777	3	3	3	3	1529	7	4	3	2	101	12	50
1987	Brussels	777	5	3	5	3	2273	9	6	5	4	101	12	50
1986*	Harrow	0	0	0	0	0	199	0	0	0	0	54	0	53
1986	Ridgetowr	0	0	0	0	0	199	0	0	0	0	54	0	13
1986	Huron Park	514	3	2	1	0	1004	6	3	2	0	90	2	33
1986	Kippen	397	2	1	1	0	642	3	2	1	0	77	1	8
1986	Brussels	397	2	1	1	0	302	3	2	1	0	77	1	15
1985	Harrow	250	0	0	0	0	250	0	0	0	0	66	0	26
1985	Ridgetowr	250	0	0	0	0	250	0	0	0	0	66	0	37
1985	Huron Park	646	3	3	3	0	1268	7	5	3	2	91	5	46
1985	Brussels	659	4	3	3	0	1198	7	5	4	2	92	6	10

* Two outlier results removed for regression analysis (Harrow 1986 and Huron Park 1987).

Figure 8.5: Foliar injury to white bean in Ontario and short-term SUM60 and hourly ozone (1985-95)

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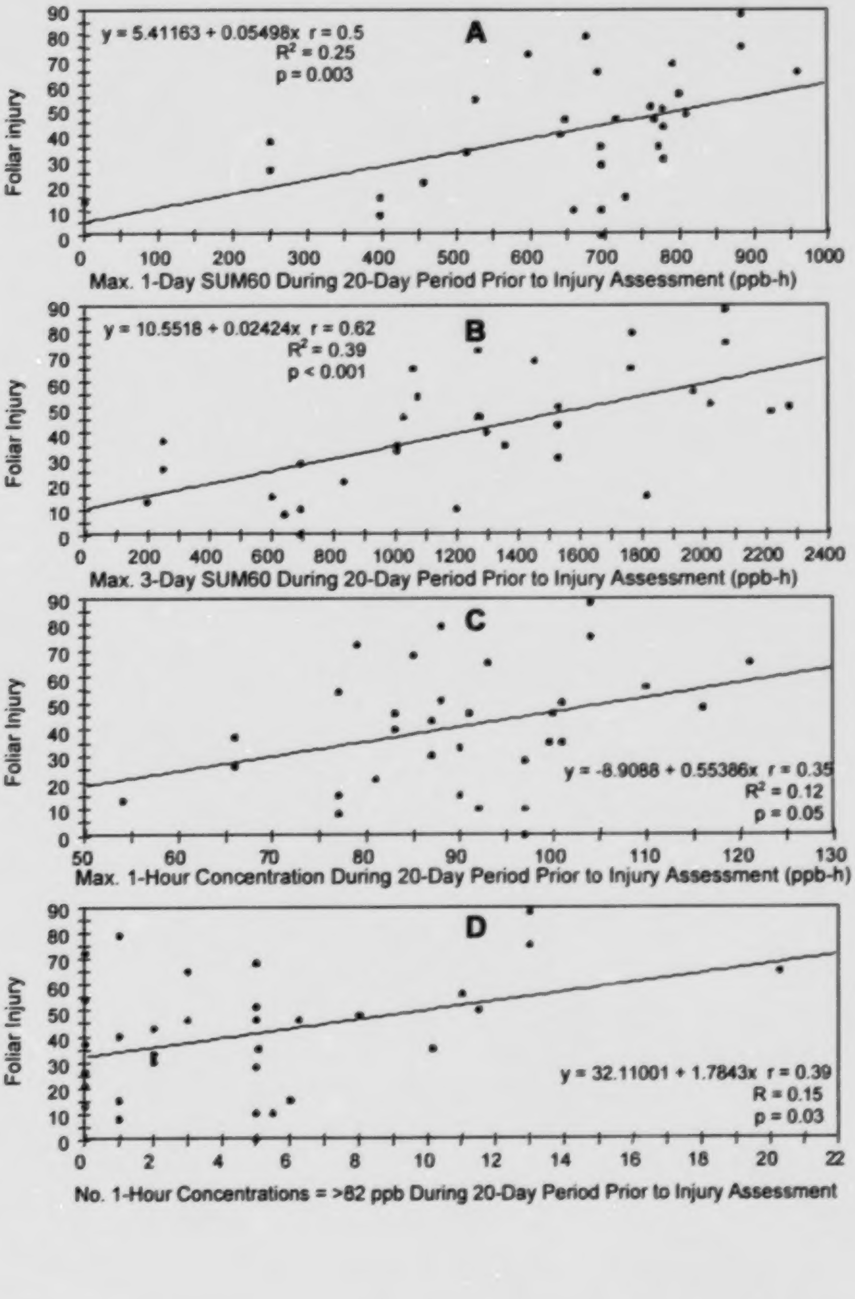


This analysis confirmed the 1995 findings, in which the 3-day SUM60 index performed the best as an indicator of air quality associated with foliar injury development ($p < 0.001$ and an R^2 of 39%); however, statistically significant relationships also were recorded for the 1-day SUM60 ($p < 0.01$) and the number of exceedances of the 1-hour objective of 82 ppb ($p = 0.03$), although the latter two indices attributed a considerably smaller percentage of injury severity to ozone, with R^2 values of 25 and 15%, respectively.

In summary, the foliar injury to white bean crops in southwestern Ontario was found to be very significantly related to cumulative ozone exposure over a three-day period during the three week (20-day) period prior to injury assessment as measured by the 3-day SUM60 index. The next best descriptor of foliar injury during this 20-day period was a one-day SUM60. Both were clearly superior (in terms of the relationship between injury severity and ozone air quality) to a count of 1-hour exceedances of the existing ozone objective of 82 ppb and from a biological perspective, this was not unexpected, given the cumulative manner in which ozone is taken up by plant foliage and metabolized. It is clearly a more biologically relevant scenario than is the number of exceedances of a certain 1-hour threshold (e.g. a level of 82 ppb) which implies that plants suddenly become sensitive and develop injury after exposure to very short peak exposures. However, the longer averaging period for the SUM60 index does not capture all of the biologcally relevant aspects of plant exposure to pollutants, though the SUM60 form itself performed reasonably well.

These findings are consistent with the early publications dealing with ozone injury to this crop (Weaver & Jackson, 1968; Haas, 1970, and Curtis et al., 1975) and point to the need for a short-term, episode-based indicator of ozone air quality.

8.2.5 Exposure Response Relationships for Acute Effects

The 1995 white bean foliar injury – ozone air quality study referred to in the previous section, besides assessing the relative value of alternative exposure indices, also shed some light on exposure-response relationships. Figure 8.4B demonstrates the relationship between white bean foliar injury, measured using the foliar injury index described earlier, and ozone exposure, measured with the 3-day SUM60. A trace level of foliar injury (foliar injury index score of 1-20) is the lowest level of injury that can be reliably quantified and is therefore a suitable assessment endpoint. Based on this analysis, the following conclusions can be made:

- a 3-day SUM60 of 500-700 ppb-h is associated with a trace injury level (foliar injury index less than or equal to 20)

Therefore, based on the 1995 white bean analysis, a LOAEL in the range of 500-700 ppb-h (3-day SUM60) is identified.

Further evaluation of the relationship between foliar injury severity on white beans and the 3-day SUM60 was done for the period 1985 - 1995. In the previous 1995 assessment, the maximum 3-day SUM60 during the 20-day period prior to assessment was selected for evaluation against foliar injury severity. In the second phase of this assessment, the relationship between the 3-day

SUM60 was explored on an exceedance basis in an attempt to determine the most appropriate concentration to provide short-term protection. This analysis of the 1985-95 white bean injury assessment included the following scenario:

- number of exceedances of 3-day SUM60 values of 500, 700, 900 and 1,100 ppb-h during the previous 20-day period.

The results of the statistical analysis are plotted in Figure 8.6. Again, detailed statistical analyses can be found in the Report of the Vegetation Working Group (Multistakeholder NO_x/VOC Science Program, 1997, VOWG). The following conclusions were drawn from this analysis:

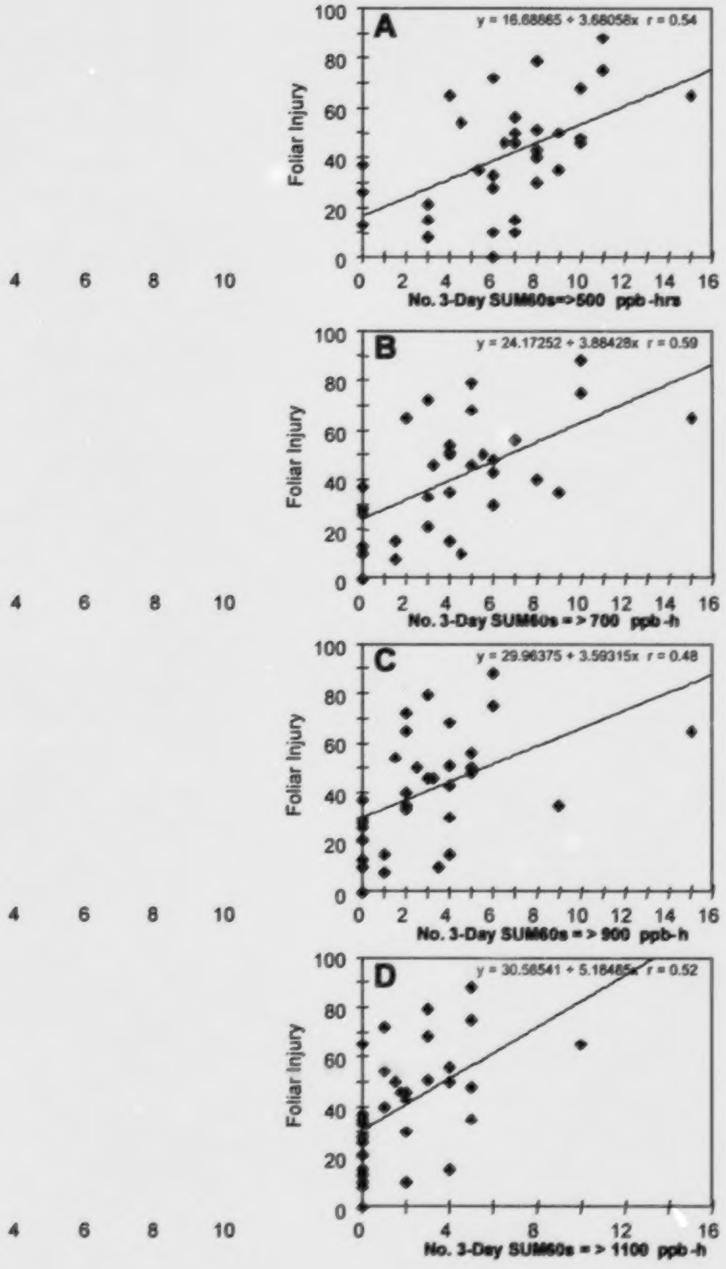
- the relationship between exceedances of a range of candidate 3-day SUM60 levels and foliar injury was highest at 700 ppb-h (scatter plot B) followed by 500 ppb-h (scatter plot A);
- the evaluation of a short-term index from an exceedance basis reveals considerable variability in the relationship with foliar injury; however, from the scatter plots, it is apparent that as the level of the 3-day SUM60 is increased from 500-1,100 ppb-h, the number of cases where greater than a trace level of injury (Foliar Injury Index > 20) occurs, with zero exceedances of the candidate SUM60 value, also increases; this provides support for a 3-day SUM60 value at the lower end of the proposed range (i.e., 500-700 ppb-h).

Therefore, a LOAEL range for trace foliar injury is identified as follows:

- A rolling 3-day SUM60 during the daily 12-hour daylight period (08:00- 19:59) for the months of April-September in the range of 500 - 700 ppb-h.

- Although both the form of the 3-day SUM60 index and the LOAEL range for acute effects have been developed on the basis of analysis of only two crops (radish and white bean) in this assessment, both of these plants are known to be sensitive to foliar injury development and to be significantly impacted as a direct result of the foliar injury.

Figure 8.6 Relationship Between Exceedances of the 3-day SUM60 and Foliar Injury to White Bean in Ontario (1985-95)



8.3 EXPOSURE ASSESSMENT FOR VEGETATION

Chapter 5 (section 5.3) of this document described the monitoring network for ground-level ozone across Canada and ambient concentrations in a regional context. As mentioned in Chapter 5, there are far more urban monitoring sites than rural or remote sites. The resulting lack of ambient data for non-urban areas is a limitation to any exposure assessment for Canadian agricultural crops or forests to ground-level ozone.

Ground-level ozone is monitored on a continuous basis and data archived as one hour averages. For the purpose of assessing ground-level ozone exposure to vegetation the data from non-urban sites are used to calculate three-month and three-day SUM60 values for rural and forested sites in Canada during 1985-93. This is summarized in Figures 8.7 and 8.8. The percentile data for these sites are shown in Table 8.15.

Figure 8.7 Frequency of 3-Month SUM60 Values at Rural and Forest Sites in Canada (1985-1993)

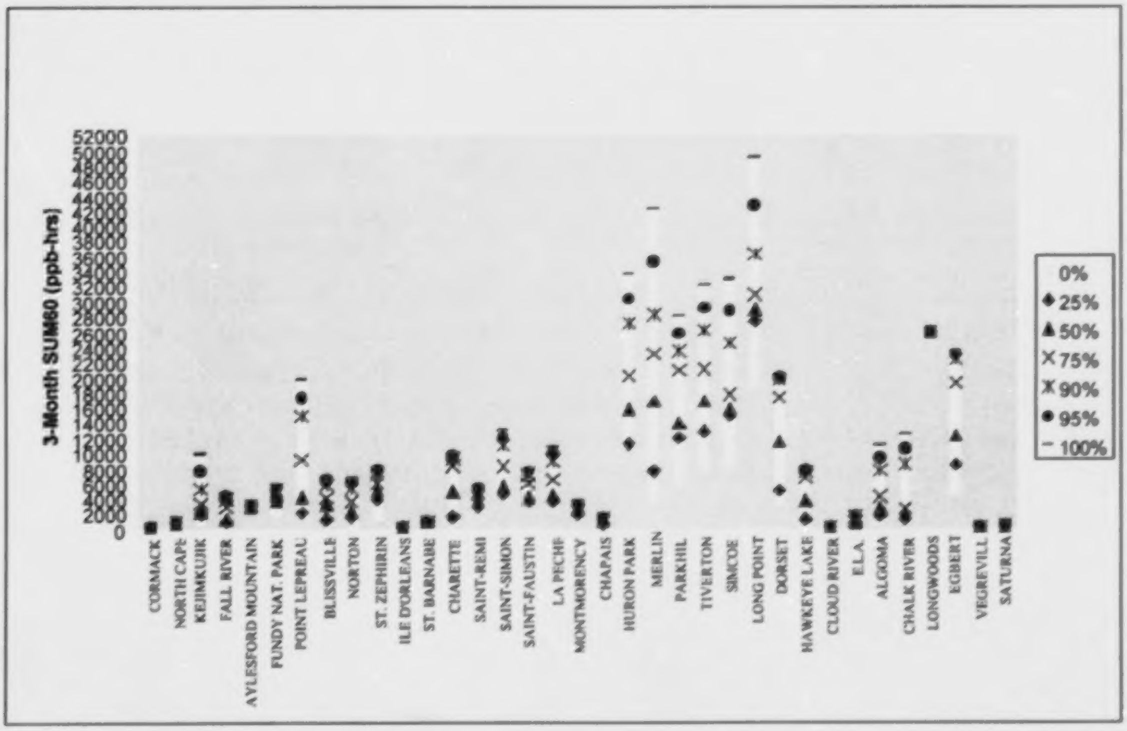


Figure 8.8 Frequency profile of 3-day SUM60 values at rural and forest sites in Canada (1985-1993)

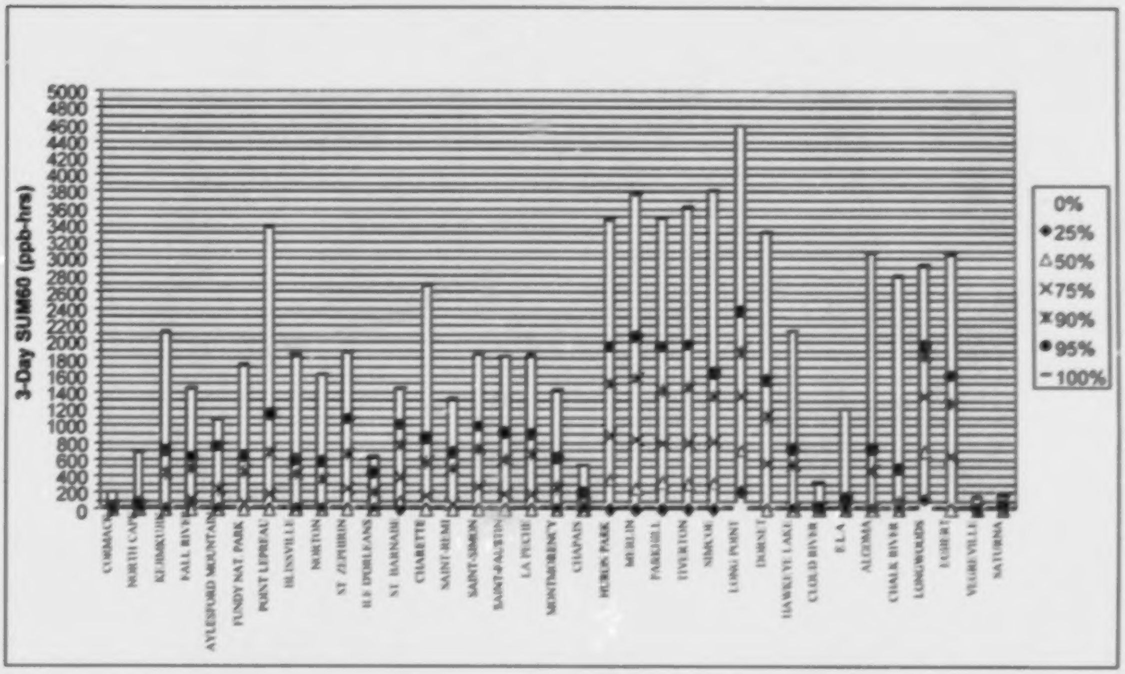


Table 8.15 Frequency profile for 3-day and 3-month SUM60 values at rural/forest sites in Canada (1985-1993)

NAPS ID	Location	Frequency Profile - 3-DaySUM60							Frequency Profile - 3-Month (June-August) SUM60						
		0%	25%	50%	75%	90%	95%	100%	0%	25%	50%	75%	90%	95%	100%
10201	CORMACK, NF	0	0	0	0	0	15	200	120	123	125	133	138	140	141
20201	NORTH CAPE, PEI	0	0	0	0	0	66	679	805	805	805	805	805	805	805
30501	KEJIMKUJIK, NS	0	0	0	0	430	694	2117	335	1985	2223	3278	5245	7541	9836
30601	FALL RIVER, NS	0	0	0	122	485	622	1442	587	897	1208	2904	3922	4261	4600
30701	AYLESFORD MOUNTAIN, NS	0	0	0	0	237	751	1064	2717	2820	2922	3024	3086	3106	3127
40401	FUNDY NAT. PARK, NB	0	0	0	61	451	627	1729	1649	3564	3637	4658	5076	5215	5354
40501	POINT LEPREAU, NB	0	0	0	180	679	1135	3384	1506	2118	4161	9016	14845	17164	19484
40601	BLISSVILLE, NB	0	0	0	0	412	580	1840	795	1197	3211	4036	5699	6254	6808
40701	NORTON, NB	0	0	0	0	349	563	1613	0	1494	2207	3465	5345	5971	6598
51501	ST. ZEPHIRIN, QC	0	0	0	252	660	1077	1870	952	3737	4996	5998	7206	7608	8011
51601	ILE D'ORLEANS, QC	0	0	0	0	206	439	621	160	160	160	160	160	160	160
51701	ST. BARNABE, QC	0	0	93	386	770	1015	1441	856	856	856	856	856	856	856
52001	CHARETTE, QC	0	0	0	151	563	850	2690	211	1508	4827	8252	9222	9545	9868
52101	SAINT-REMI, QC	0	0	0	60	487	673	1312	2130	2896	3662	4429	4888	5042	5195
52201	SAINT-SIMON, QC	0	0	0	270	720	993	1850	4200	4419	5568	8173	10926	11843	12760
52301	SAINT-FAUSTIN, QC	0	0	0	185	590	910	1830	3130	3611	4091	5949	7064	7436	7807
52401	LA PECHE, QC	0	0	0	180	660	889	1840	2529	3537	4406	6360	8915	9766	10618
54001	MONTMORENCY, QC	0	0	0	0	258	615	1428	1586	1829	2423	2533	2890	3057	3224

Table 8.15 (cont'd) Frequency profile for 3-day and 3-month SUM60 values at rural/forest sites in Canada (1985-1993)

NAPS ID	Location	Frequency Profile - 3-DaySUM60							Frequency Profile - 3-Month (June-August) SUM60						
		0%	25%	50%	75%	90%	95%	100%	0%	25%	50%	75%	90%	95%	100%
54201	CHAPAIS, QC	0	0	0	0	60	199	530	313	586	859	1132	1296	1351	1405
62101	HURON PARK, ON	0	0	351	884	1505	1940	3463	10524	11120	15630	20038	26977	30234	33491
62201	MERLIN, ON	0	0	245	837	1566	2064	3770	2942	7518	16728	22935	28144	35144	42143
62401	PARKHILL, ON	0	0	320	790	1429	1948	3473	5250	11963	13918	20766	23364	25688	28012
62501	TIVERTON, ON	0	0	304	797	1465	1967	3620	7103	12769	16701	20956	26100	29043	31987
62601	SIMCOE, ON	0	0	308	816	1353	1628	3810	7433	14821	15799	17601	24385	28623	32862
62701	LONG POINT,ON	0	210	706	1361	1885	2372	4580	18271	27365	28877	30784	36140	42546	48951
63301	DORSET, ON	0	0	0	556	1110	1536	3312	2754	4961	11474	17181	19560	19801	20041
63401	HAWKEYE LAKE, ON	0	0	0	0	530	714	2132	0	1214	3653	6732	7368	7495	7622
63901	CLOUD RIVER, ON	0	0	0	0	0	27	313	183	183	183	183	183	183	183
64001	E.L.A., ON	0	0	0	0	0	125	1195	260	665	824	911	1504	1702	1900
64101	ALGOMA, ON	0	0	0	0	472	716	3062	517	1659	2680	4182	7708	9273	10839
64201	CHALK RIVER, ON	0	0	0	0	82	477	2788	434	1080	1932	2615	8472	10425	12377
64301	LONGWOODS, ON	0	123	692	1357	1833	1961	2923	25817	25817	25817	25817	25817	25817	25817
64401	EGBERT, ON	0	0	0	632	1267	1592	3058	3926	8297	12155	19066	22215	22747	23279
90901	VEGREVILLE, AB	0	0	0	0	0	0	145	148	148	148	148	148	148	148
102001	SATURNA. BC	0	0	0	0	0	61	164	126	146	166	285	356	379	403

8.4 RESEARCH NEEDS

There are several significant areas where additional research would provide much needed certainty for the establishment of vegetation based air quality criteria for Canada. Some of these were summarized recently by Heck and Cowling (1997) following a workshop of vegetation experts in early 1996. From a Canadian point of view, the more important areas include:

- the implementation of a fully monitored experimental open-top chamber program for crop and tree species throughout Canada, to develop dose-response relationships for Canadian species;
- review and development of vegetation exposure indices that best reflect the biologically relevant aspects of ozone exposure using Canadian experimental data, from point above;
- detailed exposure assessment to determine the severity of current impacts and anticipated risks to Canadian agricultural and tree species;
- the continued evaluation of factors influencing vegetation response to ozone, particularly those that relate to the use of air quality data as surrogates of ozone exposure at locations remote from the vegetative canopy (i.e., study of flux of ozone to plant and ecosystem canopies);
- the study of interactive effects of ozone with other plant stressors, including other oxidants, and co-occurring regional pollutants, insects, disease, drought stress, soil nutrition and factors involved in climate change;
- the investigation of how adverse effects of ozone occurring at the cellular level can be interpreted in terms of foliar or canopy-level impacts and, ultimately, effects at the ecosystem level; and
- the VOWG analysis also pointed to the need for much improved ozone-monitoring coverage in many rural and forested areas of Canada and the establishment of an experimental monitoring program to investigate the most appropriate monitoring location relative to canopy position/level.

8.5 SUMMARY

For chronic effects, LOAEL ranges were identified for both agricultural and tree species, and a LOAEL range was also identified for acute impacts on agricultural species. These were:

- 3 month SUM60 LOAEL range, at the 10% biomass loss level, of 5,900 to 7,400 ppb-h for agricultural species (see Table 8.10)
- 3 month SUM60 LOAEL range, at the 10% biomass loss level, of 4,400 to 6,600 ppb hrs for tree species (see Table 8.11)
- 3 day SUM60 LOAEL range, at the trace foliar injury level, of 500 to 700 ppb hrs for agricultural species

Given the available experimental data it was determined that the uncertainties in the data and lack of quantitative Canadian dose-response data were too great to further narrow the range and identify single numerical LOAELs for agricultural or tree species. It is recommended that when experimental data do become available that efforts be focussed on developing LOAELS for vegetation classes (e.g.: cereals, pulses, legumes, vegetables, coniferous trees, deciduous trees). The inter species variability is anticipated to be too great for the determination of a single valid LOAEL.

For the purposes of assessing ozone impacts to vegetation impacts in Canada the reader is referred to Tables 8.9 and 8.11 which present the best available species specific estimates of ozone levels at which reduced yield or biomass loss may occur.

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NATIONAL AMBIENT AIR QUALITY OBJECTIVES FOR GROUND-LEVEL OZONE

SCIENCE ASSESSMENT DOCUMENT

A Report by
the Federal-Provincial Working Group
on Air Quality Objectives
and Guidelines

July, 1999

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Part 5 of 7

Canada

9 EFFECTS ON BIRDS AND MAMMALS

Since the NO_x/VOC Science Assessment Program did not address the issue of ozone effects on wildlife or domesticated birds and mammals, an independent review of the literature, up to the end of 1996, was undertaken. This chapter reviews the effects of ozone on birds and mammals and clearly reflects the paucity of literature available. The available information does indicate though that effects are likely not negligible under episodic (i.e. high concentrations) and, perhaps, lower ambient conditions.

Information contained in journal articles and other sources of primary literature that were considered in this report were identified through the following computerized databases:

Medline
Agricola
CAB Abstracts
Life Sciences
RTECS
HSDB
PolTox

In addition, toxicological abstracts from the past ten years and biological abstracts from the last three years were examined. Current Contents, which lists papers published, was also reviewed.

9.1 DOMESTIC BIRDS

For birds, the only significant exposure route to ozone is inhalation, and exposure can be represented by the concentration of ozone in inhaled air. Information on the effects associated with exposure via inhalation is summarized below. Indirect effects of ozone on birds, for example, due to adverse effects on plants upon which birds may depend, were not considered in this review.

9.1.1 Toxicological Assessment

Ozone's biological effect is attributed to its ability to cause oxidation or peroxidation of biomolecules directly and/or via free radical reactions. A sequence of events may include lipid peroxidation and loss of functional groups of enzymes, alteration of membrane permeability, and cell injury or death (Mustafa, 1990).

There are many distinct differences between the bird's lung-air sac respiratory system and the mammalian bronchoalveolar lung. The respiratory apparatus of birds has evolved from the primitive sac-like alveolar lungs of reptiles in response to the large metabolic demands of flight. This evolutionary process has produced a respiratory system with substantial physiological differences relative to other vertebrates. Among the most important of these differences are that birds have a higher mass-specific minute ventilation, higher mass specific effective ventilation of gas-exchange tissues, cross-current and counter-current gas-exchange mechanisms and a gas diffusion barrier half the thickness of that of mammals (Brown et al., 1997). While these differences may predispose birds to greater sensitivity to inhaled toxicants, there is insufficient information to make any predictions concerning relative sensitivities. There appears to be a complex relationship between a species' respiratory physiology, its pathophysiologic response to a toxic gas and other physiologic factors. For instance, Japanese quail appear to respond to ozone exposure in a different way than mammals (Rombout et al., 1991). No signs of repair in the air capillary epithelium of Japanese quail were observed after seven days of ozone exposure, indicating that the quail lacks the morphological and biochemical repair ability observed in mammals (Rombout et al., 1991). The development of tolerance to ozone has been reported in mammals. Pre-exposure to ozone did not confer tolerance in chicks (Quilligan et al., 1958).

Three studies which examined the effects of ozone exposure to birds were identified. These studies are described below, and are summarized in Table 9.1.

Rombout et al. (1991) exposed 8-week old male Japanese quail (*Coturnix coturnix japonica*) to 0, 0.3, 1.0 and 3.0 mg/m^3 (0, 0.15, 0.50 and 1.50 ppm respectively) of ozone in closed inhalation chambers continuously for seven days. Pulmonary effects were determined by light and electron microscopy, as well as by biochemistry. Focal areas of haemorrhage were observed in the birds exposed to 0.5 ppm ozone. Loss of cilia in the trachea and bronchi, an inflammatory response, and necrosis of air capillary epithelial cells were also seen after exposure to 0.5 ppm. Following exposure to 1.50 ppm ozone, many atria of tertiary bronchi were completely obstructed by extensive haemorrhage, and metaplasia of atrial wall cells and hypertrophy of smooth muscle cells were also observed. The cilia in the airways disappeared almost completely in the1.50 ppm group. No histological differences were seen in the heart, liver, kidneys, spleen, and bursa of Fabricius between the animals of the control group and the group exposed to 1.50 ppm ozone. Lung biochemistry data revealed that in the 1.50 ppm group, lactate dehydrogenase, glucose-6-phosphate dehydrogenase and glutathione reductase activities were significantly increased. No effects on lung antioxidant enzymes were observed in the 0.15 and 0.50 ppm exposure groups.

Table 9.1 Summary of Scientific Studies and Results for Ozone Effects on Domestic Birds

Study author(s), year, journal	Species, life stage, age	Ozone concentration and exposure time	Protocol	Endpoint measured	Significant ($p < 0.05$) effect? Y/N
Rombout et al., (1991)	Japanese Quail (*Coturnix coturnix japonica*) 8-week old males	0, 0.15, 0.50 and 1.50 ppm for 7 days	Continuous exposure in closed chambers	Morphology and biochemical analyses for protein content, G6PDH, GSH-Px, GSH-Red[1]	N at 0.15 ppm Y at 0.50 ppm Y at 1.50 ppm
Bartov et al., (1981)	Crossbred New Hampshire x White Leghorn male chicks, ages ranged from 1-11 days at start of experiment	0.3 or 0.7 ppm	Continuous exposure in a closed chamber 7-21 days; fed various diets	Growth, nutritional encephalopathy, fatty acid composition of the cerebellum and lungs	No consistent effect on severity of nutritional encephalopathy. N for liver α-tocopherol content and fatty acid composition of the cerebellum. Y for increased palmitic acid in total lung lipids at 0.7 ppm, and for lung congestion in all ozone treated chicks
Quilligan et al., (1958)	Young chicks (species not specified)	1-4 ppm for 8 days (mean = 1.96 ± 0.19 ppm)	Continuous exposure	Death	Y: mean survival time = 1.2 days
		12-13 ppm for 3.5 to 5.5 hour intervals	Limited acute exposure	Death	Y

[1] 6PDH = glucose-6-phosphate dehydrogenase; GSH-Px = glutathione peroxidase; GSH-Red = glutathione reductase

The effect of ozone on the development of nutritional encephalopathy, one of the vitamin E-deficiency symptoms in chicks, was evaluated by Bartov et al., (1981). Young crossbred New Hampshire x White Leghorn male chicks, receiving diets low in vitamin E and containing a source of linoleic acid, were exposed at various ages to 0, 0.3 and 0.7 ppm ozone for various time periods. No consistent effect was established on the severity of the nutritional encephalopathy. Ozone had no clear effect on the liver α-tocopherol content of chicks fed vitamin E-supplemented diets, nor did it affect the fatty acid composition of the cerebellum. However, in all cases, ozone increased the proportion of palmitic acid in total lung lipids. On macroscopic examination, all ozone-treated chicks showed congested lungs of a darkened colour. Microscopic examination showed haemorrhage within the bronchi and alveoli. In addition, abundant leukocytes were seen. Ozone exposure to 0.3 ppm and 0.7 ppm improved the weight gain of young chicks, provided that exposure was started on the day of hatching. When exposure was begun one week or later after hatching, ozone either inhibited weight gain or had no effect. The authors speculate that the growth promotion of ozone-exposed chicks could be due either to a disinfecting effect of ozone or, since accelerated growth is associated with a higher rate of protein degradation and turnover, ozone-induced enhanced protein turnover and consequently increased growth rates (Bartov et al., 1981).

In an early study, (Quilligan et al., 1958), newly hatched chicks died after three days of continuous exposure to 1-4 ppm ozone (mean ozone concentration = 1.96 ± 0.19 ppm, mean survival time = 1.2 days). The pathological findings were principally those of edema and haemorrhage of the lungs. In an additional experiment in which ozone concentrations were kept constant and the exposure time varied, an LD50 of 53.5 ppm-hours was calculated, which corresponds to 8.9 ppm for a six-hour exposure. In a final series of experiments, several conditions of pre-exposure and challenge were studied. No evidence of tolerance on re-exposure of chicks to ozone could be demonstrated (Quilligan et al., 1958).

Table 9.2 outlines the effects reported and scores them according to the frequency and consistency of occurrence in the studies reviewed.

Table 9.2 Categories of Effects and Scores

Effect	Score[1]	Comment
Reduced growth and/or weight gain	-	One study found growth enhanced following exposure to ozone at a specific time of growth; exposure beyond that age had no effect or a negative effect.
Reduced reproductive vitality	-	Effect not measured in the studies reviewed.
Increased susceptibility to pathogens	+	Increased presence of leukocytes found in one study, significance not clear.
Increased susceptibility to physical stressors	+++	Hemorrhage found in the lungs of test animals in all studies.
Mortality	++	One study examined mortality as an endpoint. Effect found at various concentration/duration combinations.

[1] scores range from - (effect not found/not reported) to +++ (effect consistently found over various exposure scenarios)

Based on this analysis, increased susceptibility to physical stressors (in this case, lung hemorrhage) is the most appropriate endpoint for which adequate data is available to identify an effect level. Although lung hemorrhage is consistently found, little information on other potential relevant endpoints is available. This adds uncertainty to the selection of the endpoint. Other sources of uncertainty include the lack of information documenting ozone's effects on wild birds; the fact that all of the captive domestic birds in these studies had no flight exercise, therefore it is difficult to extrapolate these results to wild avifauna; and the lack of information on the effectiveness of the avian respiratory tract repair mechanism. Lung hemorrhage still appears to be the most appropriate dose-response metric, however, as it was consistently found and was the most sensitive endpoint from the reviewed studies.

9.1.2 Summary

Three studies were reviewed that studied the effects of ozone on birds. These included one which examined the acute lethal effects of ozone to chicks, a second which examined the effects on growth, nutritional encephalopathy and fatty acid composition of chicks following continuous exposure to 0.3 or 0.7 ppm ozone for 7-21 days, and another which examined the morphology and biochemical changes in Japanese quail exposed to 0.15, 0.50 and 1.50 ppm ozone for seven days.

Lung haemorrhage was noted in all of the studies. Lung haemorrhage was seen in chicks exposed to 0.3 ppm and in Japanese quail exposed to 0.50 ppm, but not when exposed to 0.15 ppm. There are insufficient data to identify the potential effects to birds due to chronic exposure to ozone. In addition, no data were identified which examined the effects of ozone on wild birds. The Quilligan et al. (1958) study examined the lethal effects of acute exposure to ozone, which is not an appropriate endpoint for ambient exposures, which are typically chronic and low level.

The major differences between avian and mammalian lung systems make it difficult to extrapolate mammalian findings to birds. Avian lungs may respond differently, both qualitatively and quantitatively, to oxidant gas exposure than lungs from mammalian species for several reasons. The gas exchange area per unit body weight is small in birds compared to mammals, since birds possess a higher surface area to body weight ratio. Furthermore, birds have a higher diffusing capacity than mammals that accommodates the high metabolic rate during flight, resulting in a higher demand for oxygen. The consequent high respiration rate leads to an increased ozone flux to the tissue when ozone polluted air is inhaled. Unlike some experimental mammals, birds do not appear to develop tolerance to ozone exposure and some birds, such as Japanese quail, lack the morphological and biochemical repair ability seen in mammals. The unknown effectiveness of avian repair mechanisms in the respiratory tract constitutes yet another highly uncertain element in the qualitative risk assessment of ozone exposure of birds.

In conclusion, to protect domestic birds from short-term adverse effects, ambient ozone concentrations should not exceed 0.15 ppm. The potential effects to birds due to chronic exposure to ozone are unknown. The damage induced by ozone in the gas exchange area of avian lungs, together with the apparent lack of adequate morphological and biochemical repair capacity, gives rise to concern regarding the potential health effects on this order of animals.

9.2 DOMESTIC MAMMALS

As for birds, the only significant exposure route for mammals is inhalation, and exposure can therefore be defined as the concentration of ozone in inhaled air. Information on the direct effects associated with exposure via inhalation is summarized in the following sections. Indirect routes of exposure, for instance adverse effects on plants upon which mammals may depend, were not considered in this review.

9.2.1 Toxicological Assessment

Ozone's biological effect is attributed to its ability to cause oxidation or peroxidation of biomolecules directly and/or via free radical reactions. A sequence of events may include lipid peroxidation and loss of functional groups of enzymes, alteration of membrane permeability, and cell injury or death. Acute exposure to ozone causes lung injury involving the ciliated cells in the airways and the type 1 epithelial cells in the alveolar region. The effects are particularly localized at the junction of the terminal bronchioles and alveolar ducts (Mustafa, 1990). In a typical short-term exposure, the lung tissue response is biphasic: an initial injury-phase characterized by cell damage and loss of enzyme activities, followed by a repair-phase associated with increased metabolic activities, which coincide with a proliferation of metabolically active cells, for example the alveolar type 2 cells and the bronchiolar Clara cells (Mustafa, 1990).

Eleven studies which examined the effects of ozone on domestic mammals were identified (Table 9.3). These could be subdivided into three categories: one study examined the adverse developmental effects of exposure to ozone, three examined the effects on red blood cells (RBC) and seven examined inflammatory responses. No studies were found which examined the effects of ozone on wild mammals. Most of the literature on domestic mammals examined the effects of ozone on sheep. This is most likely due to the potential use of this animal model as a surrogate for human studies. For instance, the Dorset sheep has an erythrocyte G-6-PD activity that is very low, being comparable to human A-variants with G-6-PD deficiency (Moore et al., 1981) and sheep generally have airway responses to noxious stimuli which tend to mimic human responses arising from allergic challenge or irritative stimuli (Allgera et al., 1991). In addition, the adult body weight of the ewe is 40-60 kg, comparable to humans, thus making techniques for comparing results to humans more easily applied. One study was found regarding effects on horses, one regarding *in vitro* effects on the erythrocytes of cows and pigs and one study which examined the effects on ferret tracheal glands.

Developmental Effects:

Exposure to ozone (1 ppm for 4 hours/day for 5 days) during the first week after birth retarded the normal development of the tracheal epithelium in lambs. Mucus and ciliated cell percentages remained at new-born levels in treated lambs, indicating that ozone exposure during the first week of life retards the normal development of the mucociliary system in sheep, which may lead to prolonged impairment of lung mucociliary clearance and thus increase the incidence of chronic obstructive airway disease in adulthood (Mariassy et al., 1990). Mucociliary clearance removes particles and cellular debris from the conducting airways. Impairment of this system could prolong the retention of unwanted materials (e.g., inhaled particles) in the lungs, allowing them to exert their toxicity or physical damage for longer periods of time.

Effects on Red Blood Cells

Although a statistically significant biochemical change (i.e., a decrease in glutathione levels) was noted only at the 0.5 ppm level, ozone was found capable of producing systemic oxidant stress on the red blood cells of female sheep at concentrations as low as 0.12 ppm (Moore et al., 1984).

Ozone exposure may also adversely effect red blood cell survival. Female Dorset sheep exposed to 0.25 ppm ozone showed a significant decrease in hematocrit levels (Moore et al., 1981). This decrease was not noted in the 0.50 or 0.70 ppm exposure level. The authors hypothesize that the production of excess mucus at higher ozone exposure levels may act to decrease the effective concentration of ozone reaching the lungs, passing through the air/blood barrier and consequently stressing the red cells. The 0.25 ppm ozone concentration may have minimally elicited this mucus response such that higher concentrations of ozone actually contacted the red cells (Moore et al., 1981).

An *in vitro* investigation of bovine and porcine erythrocytes exposed to ozone in the presence and absence of uric acid, a free radical scavenger, found a reduction in hemolysis and methemoglobin formation in the presence of uric acid (Meadows and Smith, 1987).

Inflammatory Response

Exposure of female sheep (aged 1-2 years) to 0.5 ppm ozone for two hours resulted in an increased number of mast cells and lymphocytes in lavage fluid when compared to controls (Sielczak et al., 1983). The increase in the number of luminal mast cells and lymphocytes following ozone exposure signals an enhanced inflammatory response in the airways. These changes could contribute to ozone-induced non-specific airway hyper-responsiveness and susceptibility to allergic IgE-mediated airway reactions (Sielczak et al., 1983).

Both short-term clearance (mucociliary) and long-term clearance (alveolar) were depressed by ozone in a dose-dependent fashion in female sheep following exposure to 1.0 ppm for 2 hours and for 5 hours per day for 4 days, respectively (Allgera et al., 1991). Ozone caused a dose-dependent decrease in tracheal mucus velocity (TMV), a marker of mucociliary function. Ciliary function, measured by Ciliary beat frequency *in vitro*, was not found to be defective, suggesting that ozone-induced mucociliary dysfunction resulted from alterations in mucus secretion (Allgera et al., 1981). Pre-treatment with N-acetylcysteine, a mucolytic substance with antioxidant activity, significantly protected the sheep from TMV decreases.

Abraham et al., (1984) investigated the relationship between airway responsiveness and the permeability of histamine through the airways in female sheep after exposure to either 0.5 or 1.0 ppm ozone for two hours. Increased airway responsiveness and airway permeability were observed in the sheep exposed to 0.5 ppm. Approximately half of the sheep exposed to 1.0 ppm ozone showed increases in airway responsiveness and airway permeability; the other half showed decreases in these measures. The authors concluded that since ozone-induced directional changes in airway responsiveness paralleled the directional changes in airway permeability in both the positive and negative directions, that changes in airway responsiveness to inhaled histamine following exposure to ozone may be related to concomitant changes in airway permeability to this agent.

The acute exposure of female sheep to 3-4 ppm ozone for 3 hours was associated with dose-related increases in bronchial artery blood flow (Q_{br}), an acute inflammatory response (Schelegle, et al., 1990). Another study confirmed that exposure to 3.5 ppm ozone for 3 hours induced an increase in systemic blood flow to the lung and also found that exposure to 3.5 ppm ozone plus the corticosteroid methylprednisone for 3 hours completely blocked this vasodilatory response (Gunther et al., 1992).

Horses exposed to 0.5 ppm ozone for 12 hours showed a significant increase in reduced glutathione (GSH), glutathione disulfide (GSSG), the glutathione redox ratio (GRR = GSSG/[GSH + GSSG]) and total iron concentrations in bronchoalveolar fluid (Mills et al., 1996). Reduced GSH is the primary mechanism for the removal of hydrogen peroxide in the lung. GSSG is rapidly converted back to GSH. Oxidant injury or pulmonary disease will markedly increase GSSG concentration and is one of the most sensitive assays of oxidant injury. The authors conclude that oxidant injury in the lung will induce changes in the GSH status and iron homeostasis that could affect pathogenesis of respiratory tract diseases.

Ferrets exposed to 1 ppm ozone 24-hours per day for 3 days exhibited increased basal secretion of glycoconjugates. (McBride et al., 1991). The basal secretion by tracheal glands was not significantly different from controls following exposure to 1 ppm ozone for 7 days (McBride et al., 1991). To assess the oxidant stress on tracheal gland responsiveness to cholinergic stimulation, EC_{50} values, slopes and maximal responses were determined from individual dose-response curves to carbachol. The mean EC_{50} values were significantly lower in the ozone-exposed groups compared to controls, slopes of the dose-response curves did not change and maximal secretory responses were elevated, but not significantly different compared to controls (McBride et al., 1991).

Table 9.3 Summary of Scientific Studies and Results for Ozone Effects on Mammals

Study author(s), year, journal	Species, life stage, age	Ozone concentration, and exposure time	Protocol	Endpoint measured	Significant ($p = 0.05$) effect? Y/N
Mariassy et al. (1990)	Lambs	1.0 ppm 4 hours/day for 5 days during the first week of life	For TMV^1 study, measurements were obtained at birth and after exposure. TMV was re-measured at 2, 4, 8, 16 and 24 weeks in control and exposure groups; Secretory functions, bioelectric properties and morphological assessments were made at birth and at 2 weeks.	TMV (*in vivo*), tracheal secretory function (*in vitro*), morphology of tracheal mucosa	Y, TMV decreased, N for macromolecule secretion but a partial prevention of the age-dependent decrease normally present, normal development of tracheal epithelium was retarded.
Moore et al. (1984)	Female Dorset Sheep aged between 1.5 and 7 years	0.12, 0.25, 0.50, 0.70 ppm ozone for 2.75 hours	Blood was drawn before and after ozone exposure	RBC^2 counts, G-6-PD activity, Heinz body counts, GSH, ACHE and MetHb were assayed	Y for GSH decrease at 0.50 ppm. N but a trend found for GSH decrease at 0.70 ppm, ACHE at 0.70 ppm , dose-dependent increase in MetHb, reduced RBC although no dose trend evident. G-6-PD increased up through 0.50 ppm with a slight reduction at 0.70 ppm
Moore et al. (1981).	Female Dorset sheep	0.25, 0.50 and 0.70 ppm for 2.75 hours	Blood samples tagged with Cr-51 were collected before and after ozone exposure	Effect of ozone on erythrocyte survival	Y for 0.25 ppm, N for 0.50 and 0.70 ppm
Meadows and Smith (1987)	Bovine and swine erythrocytes	Ozone flow of 1.7 µmole/min with a gas flow rate of 70 mL/min.	Erythrocyte suspensions in phosphate buffer were bubbled with ozone *in vitro* with and without uric acid.	Effect of ozone on hemolysis and methemoglobin formation of erythrocytes in the presence and absence of uric acid (an antioxidant)	Y, increase in hemolysis and methemoglobin formation with ozone; decrease in both with the addition of uric acid.
Sielczak et al., (1983)	Adult female sheep, aged 1 to 2 years	0.5 ppm for 2 hours	Lavage of a defined segment of the trachea in conacious sheep	Impact on mast cells and lymphocytes	Y, Increased mast cells and lymphocytes

Table 9.3 Cont'd Summary of Scientific Studies and Results for Ozone Effects on Mammals

Study author(s), year, journal	Species, life stage, age	Ozone concentration, and exposure time	Protocol	Endpoint measured	Significant ($p = 0.05$) effect? Y/N
Aligera et al., (1991)	Adult female sheep	1.0 ppm for 2 hours	Roentgenographic method	Impact on TMV	Y, Decreased TVM at 40 minutes and at 2 hours after exposure
		1.0 ppm for 5 hours/day for 4 days		Impact on TMV	Y, decrease the first and second day TMV was still significantly reduced 5 days after the last exposure
		Pre-treatment with NAC[3], an antioxidant	300 mg NAC administered intravenously twice a day in the 4 days prior to exposure to ozone	Effectiveness in protecting the sheep from TMV deficiency	Y
Abraham et al. (1984)	Adult female sheep	0.5 or 1.0 ppm for 2 hours, followed by a controlled 2 minute inhalation challenge with 1% histamine	Endotracheal tube for delivery of ozone, chronic carotid loop preparation for sampling arterial blood	Changes in airway responsiveness and permeability to histamine after exposure	Y
Schelegle et al. (1990)	Adult female sheep	3-4 ppm for 3 hours	Endotracheal tube for delivery of ozone, a pulsed Doppler flow transducer, secured around the common bronchial artery, to measure blood flow	Bronchial artery blood flow (an acute inflammatory response)	Y, dose-related increase in resting, unanesthetized sheep.
Gunther et al. (1992)	Adult Columbia-Suffolk female sheep	3.5 ppm for 3 hours, with and without steroids	Endotracheal tube for delivery of ozone, a pulsed Doppler flow transducer, secured around the common bronchial artery, to measure blood flow. 3 intravenous infusions of 25 mg/kg methylprednisone at 24 hr, 12 hr, and 15 min before initiation of ozone exposure	Role of corticosteroids in modulating the increase in Q_{br}[4]	Y, exposure to ozone caused increased Q_{br}, exposure to ozone and steroids blocked the increase in Q_{br}.

Table 9.3 Cont'd Summary of Scientific Studies and Results for Ozone Effects on Mammals

Study author(s), year, journal	Species, life stage, age	Ozone concentration, and exposure time	Protocol	Endpoint measured	Significant ($\rho = 0.05$) effect? Y/N
Mills et al. (1996)	Adult horses, clinically normal (n=5) or referred for poor performance (n=25)	0.5 ppm for 12 hours for clinically normal horses	Blood, tracheal wash and bronchoalveolar lavage fluid samples were collected before and after ozone exposure or from clinical cases	Impact of ozone exposure on GSH, GSSG, GRR[5] and free Fe concentrations in the body fluids examined	Y, significant increase for all parameters in bronchoalveolar fluid. N for plasma.
McBride et al. (1991).	Adult castrated males	1.0 ppm for 3 or 7 days	Animals were exposed *in vivo*, sacrificed and glycoconjugates were radio labeled and measured via liquid scintillation spectrometry	Secretory function of airway submucosal glands	Y for basal secretion of glycoconjugates after 3 days and for tracheal gland responsiveness to carbachol after 3 or 7 days.

[1] RBC = Red blood cells; G-6-PD = glucose-6-phosphate dehydrogenase; GSH = glutathione; ACHE = acetylcholinesterase; MetHb = methemoglobin;

[2] TMV = tracheal mucous velocity;

[3] NAC = N-acetylcysteine;

[4] Q_{br} = bronchial blood flow;

[5] GSSG = glutathione disulfide; GRR = glutathione redox ratio

Table 9.4 outlines the effects reported in the studies reviewed above and in Table 9.3 and scores them according to frequency and consistency of occurrence in the studies reviewed.

Table 9.4 Categories of Effects and Scores

Effect	Score[†]	Comment
Reduced growth and/or weight gain	+	One study found lambs exposed to ozone had retarded development of the tracheal epithelium
Reduced reproductive vitality	-	Effect not measured in the studies reviewed
Increased susceptibility to pathogens	-	Effect not measured in the studies reviewed
Increased susceptibility to physical stressors	+++	Three studies found adverse effects on RBC counts and biochemical evidence of oxidant stress; seven studies reported effects consistent with an inflammatory response.
Mortality	-	Effect not measured in the studies reviewed.

[†] Scores range from - (effect not found/not reported) to +++ (effect consistently found over various exposure scenarios)

Based on this analysis, increased susceptibility to physical stressors (in this case adverse effects on RBC counts/biochemical effects and inflammatory response) is the most appropriate endpoint for which adequate data is available to identify an effect level. An examination of Table 9.3 shows that of the two endpoints, adverse effects on RBC counts/biochemical effects appears to be the more sensitive endpoint, with significant effects evident at 0.25 ppm. Although this effect is consistently found and is the most sensitive endpoint from the reviewed studies, little information on other potential relevant endpoints is available and no information exists for ozone effects on wild mammals. This introduces uncertainty into the selection of the most appropriate endpoint.

9.2.2 Summary

Short-term exposure to ozone has been reported to cause adverse developmental effects, adverse effects on red blood cell counts, and inflammatory responses in domestic mammals. Adverse effects on RBC cells appeared to be the most consistent and sensitive endpoint for which effects were noted, with significant effects noted at 0.25 ppm but not at 0.12 ppm (although some evidence of oxidative stress of RBCs was observed at 0.12 ppm). The Meadows and Smith (1987) study examined the adverse effects of *in vitro* exposure of erythrocyte suspensions of cows and pigs to ozone, but this is not an appropriate endpoint for *in vivo* ambient exposures. There are insufficient data to identify the potential effects to mammals due to chronic exposure to ozone. In addition, no data were identified that examined the effects of ozone on wild mammals.

9.3 RESEARCH NEEDS

There is a notable lack of information on the effects of both acute and chronic ozone exposures on mammals and birds, both domestic and wild. More information concerning the vulnerability of birds to ozone-induced effects, and the mechanism of damage and repair of their respiratory tract during chronic exposure is required, given that there is some indication that birds may be particularly at risk.

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10 HUMAN HEALTH EFFECTS:

ANIMAL TOXICOLOGY STUDIES

A summary of the salient points from animal toxicity studies based on Bates (1994; 1995a) is provided in this chapter with an addition of studies as of April 1997. For a more comprehensive review of the work on the toxicity of ozone in animal experiments, the U.S. EPA criteria document (1996) is recommended.

10.1 BIOCHEMICAL MECHANISMS OF TOXICITY

Ozone is a potent oxidizing agent. *In vitro* experiments have demonstrated that ozone interacts with a wide variety of cellular components, including polyunsaturated lipids, antioxidants, thiols, amine groups and proteins (U.S. EPA 1986). Since ozone is highly reactive, these reactions would be expected to occur at the area of initial contact (i.e., the respiratory tract). There are virtually no data available examining the degree to which ozone itself can penetrate into tissue. It has been calculated that due to this high reactivity, ozone would, most likely, not penetrate beyond the surface mucous and surfactant fluids of the lung, except in the terminal airway regions where the epithelial cells have only minimal protection (Pryor, 1992).

Thus it has been hypothesized that a "reactive cascade", starting from interaction of ozone with the lining of the lung, forms reactive oxygen intermediates that penetrate into the cells and cause the biological effects observed. Free radicals generated from the cascade and oxygenated biomolecules that result from reaction with ozone may mediate the effects of ozone. Ozone-initiated free radical formation has been detected in rat lung tissues (Vincent *et al.,* 1996), and in rat and human blood (Liu et al., 1996, 1997), which support this "reactive cascade" notion.

With respect to target molecules, most of the attention has been centred on polyunsaturated fatty acids and carbon-carbon double bonds as the prime targets of ozone. Reactions with sulfhydryl, amino, and some electron-rich compounds may be equally important. Damages on these macromolecular structures ultimately lead to cell injury and cell death.

10.2 SUMMARY, ANIMAL AND CELLULAR STUDIES

10.2.1 Ozone Dosimetry

A considerable body of work has been published in relation to ozone dosimetry during the past few years; the major conclusions include:

Although somewhat different kinetic assumptions and geometric airway data have been used, all the models indicate that in all species, the tissue dose of inhaled ozone (expressed as micrograms/square centimetre/minute per microgram of inhaled ozone) reaches a maximum in the terminal bronchiolar region. The net dose is highest at the first point of impact, namely the trachea.

The maximally affected zone, in terms of tissue dose, in the human and in the rat is the 17th generation in the airway bronchiole branching. For the human data, this was based on a tidal volume of 800 ml, and a breathing frequency of 15 breaths/minute (Overton & Miller 1988).

The effect of exercise or increased ventilation is to increase the terminal bronchiolar regional dose slightly, and to significantly increase the pulmonary regional total dose and the dose in the proximal alveolar region.

Differences between animal species have been considered in detail (Overton & Miller, 1988); discussion of these is beyond the scope of this review, except to note that humans absorb significantly more of a given concentration of airborne ozone than rodents, and this appears to give rise to an increased response per unit of ambient ozone.

Theoretical dosimetric calculations have been compared with measurements of ozone in the respiratory tract under different conditions. Gerrity et al. (1988) measured ozone uptake in the extrathoracic airways of normal subjects, and found that this was as high as 40% on inspiration, and 92% on both inspiration and expiration. Both of these values fell as respiratory rate was increased. A surprising finding was that there was only a small difference between the uptake that occurred with nose breathing and with mouth breathing. Hynes et al (1988) found little difference between nose and mouth breathing in pulmonary function response to ozone.

These studies, collectively, indicate that deposition modelling of inhaled ozone emphasizes the terminal bronchiolar and centriacinar regions as sites of maximal tissue deposition of the gas. Exercise, by increasing both the tidal volume and breathing frequency, would be expected to increase the tissue dose significantly.

10.2.2 Acute Exposures

The principal effects observed after acute exposures of a variety of species to ozone concentrations less than 1.0 ppm, are lung inflammation and changes in lung permeability; increased airway responsiveness; and increased mortality if the animal is subsequently challenged with a bacterial aerosol, such as *streptococcus zooepidemicus*, commonly seen bacteria. The initial target of ozone appears to be lung fluid lining components and cell membranes (Pryor et al.1991). Increased permeability has been demonstrated after exposure of rats to 0.12 ppm or 0.4 ppm for two days (Guth et al. 1986) or in guinea pigs exposed to 1.0 ppm for one hour (Miller et al. 1986). The increased airway responsiveness is generally considered to be a consequence of the induced inflammation. However, a recent series of experiments on an isolated rat lung preparation (Joad et al. 1993) showed that ozone was capable of increasing airway responsiveness and damaging airway epithelium in the absence of neutrophils (polymorphonuclear leukocytes or PMN), and before a microvascular leak was caused. The presence of neutrophils was shown to increase the magnitude of these effects of ozone.

The increase of mortality in mice most likely occurs when ozone exposure precedes administration of a bacterial aerosol. This is primarily due to the adverse effect of ozone on macrophage function. Experiments using *Streptococcus zooepidemicus*- infected mice have shown that 3 hours of exposure to either 0.3 or 0.8 ppm ozone led to increased mortality, which was greater in one strain of mice than in another (Gilmour et al. 1993). The difference in sensitivity was shown to be due to a difference in the sensitivity of the alveolar macrophages in the two different strains of mice. It is the phagocytic efficiency of the macrophage that is impaired by the prior ozone exposure. Ozone exposure has also been shown to decrease the T-lymphocyte and antiviral response (Jakab & Hmieleski 1988).

Evidence that ozone impairs the clearance mechanism of the lung was provided by the observation in rats that ozone exposures to base levels of 0.06 ppm, with daily excursions to 0.25 ppm, increased the retention of asbestos fibres (Pinkerton et al. 1989). This was interpreted to be attributable to interference with macrophage function.

Plopper and colleagues (1990) have pointed out that non-human primates appear to be more responsive to ozone at concentrations less than 1.0 ppm than are rats. This may be due to differences in nasal structure (and hence in delivered dose) or to differences in lung structure, since rats do not possess the many generations of respiratory bronchioles that exist in human and primate lungs.

This brief summary of the effects of acute animal exposures shown in animal experiments indicate that aggravation of inflammatory lesions and worsening of respiratory infections are effects that should be evaluated in the human population.

Other phenomena described following acute ozone exposures to animals or to cells, usually to higher concentrations than those in ambient air, include:

Morphological changes in the nasal cavity and nasopharynx;

Greater sensitivity, in general, of younger rats versus older;

No differences in effects between normal rats and rats with elastase-induced emphysema (only one study reported);

A wide range of biochemical effects, including damage on polyunsaturated fatty acids, depletion of endogenous antioxidants, and damage on proteins; and effects on the production of arachidonate metabolites (inflammation mediators);

Cardiovascular effects including reduction of heart rate, arterial blood pressure and core temperature, and increase in frequency of arrhythmia in rats (Watkinson et al., 1993; Arito et al., 1990; Uchiyama & Yokoyama, 1989)

10.2.3 Long-term exposures

Human controlled exposures for longer than a few hours are not feasible, hence the results of longer term animal exposures are very important. Since the primate lung appears to be more sensitive to ozone than does the rat lung, the evidence from primate exposures (*Macaca fascicularis*) will be considered first. Almost all of this work has originated from the Primate Centre in Davis, California. It has been elegantly summarised and well illustrated by this research group (Tyler et al. 1992). The exposures were generally to 0.25 ppm ozone for 8 hours/day, 7 days/week for 18 months. A very brief summary of their findings and conclusions follows:

1. The initial inflammatory response is modified in subsequent exposures, but inflammatory cells in the peribronchiolar connective tissues persist during exposures that last up to one year;

2. Epithelial and interstitial changes in distal airways are the most striking morphologic changes in animals exposed for a year or more. There is a proliferation of non-ciliated bronchiolar and Type 2 alveolar epithelial cells. These changes, which impair the clearing function of the lining, start early, and are evident after 50 hours of exposure to 0.8 ppm of ozone.

3. Necrosis of ciliated and type 1 pneumocytes occurs, and these cells are replaced by the cells noted in 2) above. The long-term effect is therefore a "remodelling" of the centriacinar airways by extension of bronchiolar cell types in airways that were formerly alveolar ducts.

4. There is an increase of collagen localized in the peribronchiolar and centriacinar regions. This confirms earlier studies from the same laboratory in rats exposed to higher concentrations of ozone.

5. The morphological changes induced by the ozone exposure were still present after a 6 month post-exposure period of living in filtered air. Quantitative morphology studies indicated that the lungs were more abnormal after the post exposure period than immediately after the ozone exposure.

Rat exposures of longer than 2 weeks have been studied in a number of centres. Using a 78 week exposure protocol of a base exposure of 0.06 ppm with spikes to 0.25 ppm, Chang et al. (1992) showed that an acute response occurred in the centriacinar region; that these changes partly resolved that Type 2 cells increased; that the interstitium was increased; that the basement membrane was thickened; but that centriacinar remodelling did not occur. Earlier observations from the same laboratory using a 6 week exposure protocol of similar concentrations (Barry et al. 1988) had noted that there was an increase in interstitium thickness, and an increase in number of alveolar macrophages. Rat exposures to 0.95 ppm for 8 hours/day for 90 days were found by Barr et al. (1988) to have resulted in airway remodelling, and the lesions resulting from chronic versus daily episodic exposures were similar (Barr et al. 1990).

Costa et al. (1988) were able to demonstrate changes in lung function in rats after brief exposures, and in a more recent paper reported reductions in forced vital capacity (FVC) of rats after repetitive ozone exposures (Costa et al. 1994).

Saldiva et al (1992) in Sao Paolo exposed 60 rats for 6 months to the ambient air, and compared them to controls kept for the same length of time in a clean area. A monitoring station 200 metres from the exposure location showed that ozone went up to 0.4 ppm; particulates up to 90 $\mu g/m^3$; SO_2 up to 0.025 ppm; and CO up to 4 ppm. The exposed rats had secretory cell hyperplasia in the airways, ultrastructural cilliary alterations, and a more rigid mucus, changes that caused mucociliary clearance impairment. Nasal resistance and inflammatory cells in bronchoalveolar lavage (BAL) were also increased in the exposed group.

Genotoxicity, mutagenicity, and effects on carcinogenicity have also been observed. Although such effects can be shown, for instance on deoxyribonucleic acid (Hamelin 1985), there is no human correlate. Witschi (1988) reviewed these observations, pointing out that the radiomimetic activity of ozone did make it a potential contributor to human lung cancer.

10.2.4 Ozone in combination with other chemicals

Since human exposures are rarely to a single pollutant, the question of interaction with other chemicals assumes some importance. In very detailed experiments on rats, Last (1990) studied the effects of ozone and sulphuric acid aerosol alone and in combination. On all outcomes related to an inflammatory response, the two were additive in their effects, but were not clearly synergistic. Nishikawa et al. (1992) studied the effects of ozone and cigarette smoke in guinea pigs. They showed that airway responsiveness and permeability were affected when both irritants were inhaled, although single exposures to each separately at the same concentration produced no effect. This suggests that there may be a synergistic effect.

10.2.5 Applicability of animal toxicity studies to humans

Animal exposures are valuable for elucidating mechanisms of action; although recent human experimentation using bronchial lavage and even bronchial biopsies have added to this knowledge. Animal exposure data in relation to the effects of longer term exposures are of more contemporary importance, as human clinical studies of that phenomenon are impractical, and epidemiological studies of chronically exposed populations are few at present and usually involve co-exposure to other chemical substances.

The question of "biological plausibility" in reaching a judgement of causality, is complex. It requires consideration of dosimetry; of physiological and biochemical differences between species; and of the pathology and pathophysiology of common conditions such as asthma. A recent comparative dosimetric study has provided some very interesting and valuable data in this respect. Hatch et al. (1994) exposed both human subjects (with intermittent exercise) and resting rats to 400 ppb ^{18}O-labelled (a stable isotope of oxygen) ozone for 2 hours. Another group of rats was exposed to 2000 ppb ^{18}O-labelled ozone. The researchers analyzed the amount of recovered ^{18}O in bronchoalveolar lavagable cells from the human subjects and the rats. Data demonstrate that the exercising humans had four- to five-fold higher ^{18}O concentrations in all of their bronchioalveolar lavage constituents than did the resting rats. The humans also had significant increases in all of the airway inflammatory markers after 400 ppb ozone, whereas the rats did not. Rats that were exposed to 2000 ppb ^{18}O-labelled ozone had levels of ^{18}O in bronchoalveolar lavage that were more comparable to but still lower than those of humans. A detailed analysis of the distribution of ^{18}O-labelled ozone in rats shows that 49.6% was taken up by the head, 6.7% by the larynx/trachea, and 43.6% by the lungs (Hatch et al., 1989).

These studies provide a dose and effect linkage between rats and humans, which should assist in extrapolating animal toxicity data to humans. When taking into account the much lower sensitivity of rats to ozone in comparison with that of humans, it is conceivable that the doses used in experimental animals (as low as 100 ppb) that produced pathological changes are similar to the concentrations encountered by human population during ozone episodes. When ozone is delivered into deep airways, the relationship between the pulmonary tissue dose (normalized to body weight) and the pulmonary inflammation (measured as bronchoalveolar lavage protein) among rats, guinea pigs, rabbits and humans is approximately in the same pattern (US EPA, 1996).

With respect to regulatory issues such as establishment of objectives, exposure response data from animal studies on rodents are of value qualitatively, since all species appear to respond similarly, but they are of limited use quantitatively due to differences in morphology of both the nose and the bronchial tree/lung area. These lead to a difference (reduction) in net uptake of inhaled ozone in rodents and a resulting reduction of response for a given concentration of ozone in rodents compared to primates, assuming the same time of exposure and ventilation rate.

10.3 RESEARCH NEEDS

- Few studies have demonstrated cardiorespiratory effects at ozone concentrations below 0.12 ppm, although epidemiological studies have shown increased mortality and morbidity below 0.12 ppm ozone. It is not clear whether failure to detect adverse effects in animals at ambient ozone concentration is because of species differences in responses to ozone, or due to the biological markers used that are not sensitive for minor injuries. It would be desirable to examine the effects of ambient levels of ozone on animals with compromised cardio-respiratory systems.

- Studies should be extended to include the effects and the mechanism of ozone on animals with asthma-like diseases or with chronic obstructive pulmonary diseases.

- More systemic effects, such as cardiovascular and developmental effects, should be investigated to elucidate the mechanism(s) of ozone-associated cardiovascular mortality observed in epidemiological studies.

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11 HUMAN HEALTH EFFECTS: CONTROLLED HUMAN STUDIES

The previous chapter presented the data of ozone studies using experimental animals, in order to elucidate the underlying mechanisms of ozone toxicity and the basic exposure–response relationships for ozone. However, whenever possible, risk assessment of pollutants should be based upon direct evidence of their health effects in the human population. Controlled human exposure studies and epidemiological studies provide extensive information on human health responses to environmental pollutants.

Controlled human exposure studies document the health effects that result from breathing known concentrations of pollutants in controlled atmospheres under laboratory atmospheric conditions. There are some advantages in performing this type of study. Since the atmosphere is highly controlled for individual pollutants, experiments can be designed to explicitly characterize the dose-response relationship. Such a controlled environment also provides the opportunity to examine interactions among pollutants or with other environmental variables such as humidity, temperature or exercise. Subjects from special groups, such as young children or elderly people, or individuals with pre-existing cardio-respiratory diseases, may also be studied to identify potentially susceptible subpopulations.

The limitations of controlled human exposure studies lie in the practical and ethical aspects of such studies. This type of study has to be limited to short duration and only to concentrations of pollutants that are expected to produce mild and transient responses. An endpoint assessment has to be relatively non-invasive, and invariably includes pulmonary function, which sometimes may not be sensitive enough to reflect the adverse effects. Furthermore, transient responses in controlled human exposure studies have never been validated as predictors of more chronic and persistent effects. Nevertheless, controlled, quantitative human studies provide a complementary approach to examine the biological plausibility of the associations that have been observed in epidemiological investigations.

The information on controlled human exposure to ozone and human response has been extensively reviewed by the United States Environmental Protection Agency (U.S. EPA) in their criteria document (1996) based on studies up to 1996. The results of their investigations were used to determine if a No Observed Adverse Effects Level (NOAEL) or Lowest Observed Adverse Effects Level (LOAEL) could be set from these data. Recently, a large body of literature on controlled human exposure studies has come to light, providing further evidence on the impacts of ambient ozone on human health.

This chapter is built upon the information from the U.S. EPA criteria document (U.S. EPA, 1996), with additional publications as of April 1997, in an attempt to assess ozone concentrations and exposure durations which impose adverse health effects on humans. Ambient air pollution is composed of a complex mixture of particulate matter and gases, therefore, potential synergistic interactions between ozone and various other pollutants are considered in this document. A key issue in the evaluation of the health effects of air pollution is to identify the individuals who are at greatest risk from exposure to air pollutants. We have, therefore, placed considerable emphasis on characterizing susceptible subpopulation(s).

11.1 PULMONARY FUNCTION EFFECTS AND SYMPTOMS OF ACUTE OZONE EXPOSURE

11.1.1 Healthy Subjects

As summarized in the U.S. EPA document (1996), the major human pulmonary physiological responses to acute ozone exposure include a decreased inspiratory capacity, a mild bronchoconstriction, and a rapid shallow breathing pattern during exercise. The pulmonary function changes observed appear to act in sequence and are inter-related: the decreased inspiratory capacity results in a decrease in forced vital capacity (FVC) and total lung capacity (TLC). These effects combined with bronchoconstriction lead to a decrease in the forced expiratory volume in one second (FEV_1). Decreased FEV_1 values are closely related to decreased FVC and also to increases in airway resistance (R_{aw}). Ozone-induced pulmonary function changes demonstrate a concentration-dependent pattern.

Subjective symptoms following ozone exposure include cough, substernal soreness, and pain on deep inspiration. Other observations include airway hyperresponsiveness as demonstrated by increased physiological response to a nonspecific stimulus. The relationship between spirometry, resistance measurements, symptoms and nonspecific bronchial responsiveness is not fully determined. The weak associations suggest that several response mechanisms may be involved.

The Ozone Concentration-Response Relationship

At Rest Exposures

Since the publication of the 1996 U.S. EPA criteria document, no new studies have been reported on ozone-induced pulmonary function changes and symptoms in resting healthy individuals. The observed lowest concentration at which significant reductions in FVC and FEV_1 were reported was 0.50 ppm for a 2-hour exposure (Folinsbee et al.,1978; Horvath et al., 1979). Results on ozone-induced increase in airway resistance are inconsistent in resting human subjects at doses <1.00 ppm.

A recent study utilizing hydrogen peroxide concentration in breath as a biomarker for ozone exposure (Madden et al., 1997) did not show any significant change of hydrogen peroxide concentration following exposure of 11 resting healthy subjects to 0.4 ppm ozone for 2-hours, although the same dose of ozone caused a significant increase in breath hydrogen peroxide during intermittent exercise.

In 15 subjects with mild asthma, an 1-hour resting exposure to 0.12 ppm ozone did not initiate significant changes in pulmonary function or symptoms reported, nor did it potentiate an immediate bronchoconstrictive response to grass allergen (Ball et al., 1996).

Exposure with Exercise

Early studies on the effects of increased ventilation through exercise during ozone exposure were carried out in 1972-73 (Hazucha et al., 1973). Most of the exercise achieved a doubling of the ventilation rate. The concentration-related effects noted were decreased forced expiratory endpoints at 0.37 and 0.75 ppm. Subjective complaints included substernal soreness, chest tightness and cough. During the following years, Silverman et al. (1976) conducted further examination concerning the effects of exercise on ozone-induced pulmonary function changes. The workloads on the subjects were expressed as fraction of maximum oxygen uptake ($\underline{V}O_{2max}$), and studies were conducted at 45, 60 and 75% of $\underline{V}O_{2max}$. They found that pulmonary function responses were related to the total inhaled dose of ozone (0.37, 0.5 or 0.75 ppm, 2-hours) calculated as the product of concentration x time x $\underline{V}_E$. Moreover, exposure to increasing doses of ozone did not result in any effects on $\underline{V}O_{2max}$ or minute ventilation ($\underline{V}_E$), while the breathing frequency (f) was increased and tidal volume (V_T) was decreased at the 75% $\underline{V}O_{2max}$.

The important findings of these early studies were that at a given ozone concentration, the increase in ventilation results in increased pulmonary function responses, and that increased ventilation lowers the concentration of ozone required for a given pulmonary response. This introduces the concept of 'effective dose' which is a result of the product of the ventilation rate, the concentration of ozone and the exposure time.

McKittrick and Adams (1995) examined the effects of exercise pattern on ozone-induced changes of pulmonary function and symptoms. Twelve healthy young subjects were exposed to air or 0.3 ppm ozone for 1-hour with continuous exercise (mean $\underline{V}_E$ 60L/min), or 2-hours with intermittent exercise (mean $\underline{V}_E$ 45 to 47 L/min; protocol one with alternating 15 minutes of rest/exercise; protocol two with alternating 30 minutes of rest/exercise). The data show that FVC, FEV_1 and $FEF_{25-75\%}$ (forced expiratory flow between 25 and 75% of vital capacity) were significantly decreased after all three ozone exposure protocols. There were no significant differences in ozone-induced lung function changes among three ozone exposures, although symptom severity in the continuous exercise group was higher than in the two intermittent exercise groups. The total effective dose of ozone for the 3 protocols was not significantly different.

Subsequent studies demonstrated that an ozone concentration of 0.12 to 0.18 ppm is required to elicit significant pulmonary function decrements and increases of symptoms in healthy young adults performing moderate to severe intermittent or continuous exercises for 1 to 4-hours at $\underline{V}_E$ 30 to 90 L/min (Linn et al., 1986; Kulle et al., 1985; Schelegle and Adams, 1986; McDonnell et al., 1983; McDonnell, III et al., 1985b; Gong et al., 1986; Avol et al., 1984; McDonnell et al., 1993; Seal et al., 1993b; Balmes et al., 1996; Hazbun et al., 1993; Fox et al., 1993; Jorres et al., 1996; Aris et al., 1993; Basha et al., 1994; Foster and Stetkiewicz, 1996; Seal, et al., 1996; Aris et al., 1995; McDonnell et al., 1995; McBride et al., 1994; Liu et al., 1997b).

However, a retrospective analysis by Hazucha (1987) demonstrated that data from 2-hour ozone exposure with intermittent exercise best fit a model that was a quadratic function of the concentration of ozone. A further conclusion was that he could not define a concentration of ozone below which no pulmonary function response would be elicited (i.e., no threshold).

In order to identify personal characteristics that predict individual differences in acute pulmonary function response to ozone exposure, McDonnell et al. (1993) examined FEV_1 decrements among 290 young white male subjects (18 to 32 years old) after exposure to 0, 0.12, 0.18, 0.24, 0.3 or 0.4 ppm ozone for 2-hours with intermittent exercise ($\underline{V}_E$ • 60 to 70 L/min). Linear, quadratic, cubic and two sigmoid-shape models (the logistic and Gompertz functions) were used to describe decrements in FEV_1 as a function of ozone. The researchers found that a sigmoid-shaped concentration-response function is plausible for their data, however a stimulus 'threshold' could not be defined. Their model also predicts a decreasing response with increasing age for all nonzero ozone concentrations. For exposure to 0.4 ppm, the model predicts decrements in FEV_1 of 1.07 and 0.47 L for 18 and 30-year old subjects, respectively. They concluded that for white males, age was a significant predictor of response, with older subjects being less responsive to ozone.

In a subsequent study by the same research group (Seal et al., 1996), a less homogeneous sample population containing 371 young (18 to 35 years old) male and female, African American and white subjects was utilized. Subjects were exposed to 0, 0.12, 0.18, 0.24, 0.3, or 0.4 ppm ozone for 2.3-hours while doing intermittent exercise ($\underline{V}_E$ • 40 to 50 L/min). Personal and family histories were recorded before exposure. Lung function was recorded before, during and after exposure. Logistic function was used to model exposure-response relationship, and to test the statistical significance of age, socio-economic status, and menstrual cycle phase to the pulmonary response to ozone exposure. The overall fit of the data to the logistic model in this study was comparable to that observed by McDonnell et al. (1993). FEV_1 decrements revealed a ozone dose-dependent relationship, with a concave upward pattern over a range of low concentrations of ozone.

Individual Sensitivity

There is a large intersubject variability in response to ozone exposure. Data provided by Kulle et al. (1985) shows that in 5 subjects, exposure to ozone at doses ranging from 0.10 to 0.25 ppm for 2-hours (exercise $\underline{V}_E$ 70 L/min) resulted in no changes in FEV_1 to changes ranging from a 4% reduction to a 22% reduction, each individual having a different dose-response curve.

The factors that may contribute to this variability have not yet been defined. McDonnell et al. (1985a) studied the reproducibility of individual responses to ozone exposure (0.12 to 0.4 ppm) in healthy human subjects (18 to 30 years of age) exposed twice with intermittent exercise ($\underline{V}_E$ • 70 L/min), with from 21 to 385 days separating exposures. FVC, FEV_1, $FEF_{25-75\%}$, airway resistance, tidal volume, breathing frequency, and symptoms were monitored. The authors found a significant reproducibility in FVC, FEV_1, $FEF_{25-75\%}$, cough, airway resistance and shortness of breath at ozone concentrations ≥0.18 ppm. They concluded that the reported large intersubject variability in magnitude of response was due to large differences in the intrinsic responsiveness of individual subjects to ozone exposure.

In a recent study, Liu et al. (1997b) studied changes of plasma salicylate hydroxylation (an indicator for the production of hydroxyl radicals), pulmonary function and symptoms in young, healthy subjects following exposure to 0, 0.12, or 0.4 ppm ozone for 2-hours with intermittent exercise ($\underline{V}_E$ 45 L/min). They found that 2 out of 16 subjects had extraordinarily larger decrements of FEV_1, FEF_{50} and FEF_{75} than other subjects (>mean + 2SD), and higher plasma levels of salicylate hydroxylation (>mean + 3SD) than did other subjects. This implies that the high sensitivity of some subjects to ozone might be due to higher levels of ozone uptake or lower endogenous antioxidant defence systems in their airways.

Torres et al. (1996) studied inflammatory responses in bronchoalveolar lavage (BAL) fluid of healthy, nonsmoking responders (>15% fall in FEV_1 after ozone exposure) and non responders (<5% fall in FEV_1). Bronchoalveolar lavage fluid was obtained immediately and 18 hours after a 4-hour exposure to filtered air or 0.22 ppm ozone with exercise. Production of superoxide anion by the total lavage cell population was determined with and without phorbol myristate acetate stimulation. The concentration of polymorphonuclear leukocytes (PMN) in BAL increased nearly five fold 18 hours after ozone exposure in both responders and non-responders. In responders, stimulated superoxide anion in total cells increased progressively. Unstimulated hydrogen peroxide production in alveolar macrophages from responders decreased progressively. There were no significant changes in reactive oxygen intermediate production by cells from non-responders. The data support the observation by McDonnell et al. (1985b) who suggest that the individual sensitivity to ozone may be due largely to differences in the intrinsic responsiveness, such as macrophage function, of individual subjects to ozone.

However, a study conducted by Balmes et al. (1996) shows that ozone-induced pulmonary function changes were not correlated with airway inflammatory responses. In this study, healthy adult subjects (22 to 38 years old) were divided into least sensitive (mean ozone-induced change in FEV_1 = -7%, n = 12) and most sensitive (mean ozone-induced change in FEV_1 = -36%, n = 8) groups, and were exposed to 0.2 ppm ozone or filtered air for 2-hours during intermittent exercise ($\underline{V}_E$ • 50 L/min). Ozone exposure significantly increased airway resistance, small airway respiratory symptoms, percent neutrophils, total protein, and interleukin-8 in airway lavage fluids for all subjects combined. However, there were no significant differences between least and most sensitive groups. The data indicate that spirometric responses (such as FEV_1 and FVC) do not predict ozone-induced inflammatory changes, and may be due to separate mechanisms.

Mechanism of Acute Pulmonary Responses

It has been hypothesized that there may be an overall sequence of events influencing the outcome of ozone exposure on lung toxicity. First, ozone is delivered to the lung tissue. Second, ozone reacts with components in airway surface liquid and/or epithelial cell membranes. Third, local tissue responses including injury and inflammation are triggered. The secretion of prostaglandins may result in an inhibition of the α-adrenergic receptors which are responsible for the stimulation of the sympathetic system (relaxation of lung fibres). Finally, there is stimulation of the neural afferents (bronchial C fibres) which results in pulmonary function responses. The stimulation of C fibres, possibly through an increased sensitization of the cholinergic receptors or prostaglandins, results in the contraction of the lung smooth muscle which causes increased airway resistance and rapid shallow breathing.

An experimental animal study using isolated guinea pig lung (Joad et al., 1996) has demonstrated that acute ozone exposure increased responsiveness to methacholine, an effect which was reduced by depletion of C-fibers. The authors concluded that ozone, in the absence of systemic effects and the blood components of inflammation, increased muscarinic reactivity in part via the local effects of C-fibers.

A study conducted by Hazbun et al. (1993) has provided evidence of ozone-induced stimulation of bronchial C fibers in human subjects. In this study, healthy, nonsmoking subjects (22 to 30 years, n = 7) were exposed to filtered air and 0.25 ppm ozone for 1-hour with heavy exercise ($\underline{V}_E \cdot 60$ L/min). Their data demonstrate a significant increase in substance P, the neurotransmitter released from the afferent endings of bronchial C fiber by stimulus, in airway lavage fluids after ozone exposure in comparison with air control. This study also demonstrated that airway substance P levels were significantly correlated with an elevated airway concentration of 8-epi-prostaglandin $F_{2\alpha}$ ($r^2 = 0.89$). Lung C fibers have been shown to be stimulated by prostaglandin E_2 and other lung autacoids (Coleridge et al., 1976; Coleridge et al., 1978). Recent studies by Liu et al. (1997b) and Hazucha et al. (1996) have shown that pre-treatment with the cyclooxygenase inhibitors which inhibit the synthesis of prostaglandins, can reduce ozone-induced pulmonary function decrements in human subjects. In the study by Liu et al. (1997b) pre-treatment of acetylsalicylic acid (ASA, 0.975 g) significantly reduced 0.12 and 0.4 ppm ozone-induced increments in airway resistance, and 0.4 ppm ozone-induced decrements of peak expiratory flow rate. In the study by Hazucha et al. (1996), pre-treatment of ibuprofen (800 mg) significantly reduced 0.4 ppm ozone-induced decrements of FEV_1 and FVC, but did not alter ozone-induced increase in airway resistance. Ibuprofen pre-treatment significantly decreased post-ozone BAL levels (obtained 18 hours post exposure) of prostaglandin E_2 by 60.4%, and thromboxin B_2 by 25.5%. However, there was no correlation between post exposure prostaglandin concentrations in BAL and FEV_1 or FVC, presumably due to differences in the time courses of the development of functional and biochemical responses.

Some authors (Gerrity et al., 1994; Liu et al., 1997b) have postulated that the rapid shallow breathing may in fact be a defence mechanism that prevents ozone from reaching deep airways. Data from Gerrity et al. (1994) show that ozone-induced decrease in tidal volume (25%) is significantly correlated with a decreased ozone uptake efficiency of the lower respiratory tract. Data from Liu et al. (1997b) also demonstrate a more rapid and shallow breathing following exposure to 0.4 ppm ozone compared with exposure to air control and 0.12 ppm ozone. Concomitantly, the increase of *in vivo* hydroxyl radical production was not proportional to exposure concentrations of ozone; a threefold increase in ozone concentration did not cause an increase of hydroxyl radical production to the same extent, probably due to the modification of breathing pattern at high ozone concentration (Liu et al., 1997b). More studies are required to examine the effects of ozone responsiveness, the distribution in the airways and the resulting airway inflammation.

11.1.2 Subjects with Pre-existing Disease

This section includes subjects with (1) chronic obstructive pulmonary disease (COPD), (2) asthma, (3) allergic rhinitis, and (4) ischemic heart disease.

Subjects with Chronic Obstructive Pulmonary Disease

To summarize the U.S. EPA criteria document (1996), in previously reported studies (Linn et al., 1982a; Linn et al., 1983; Solic et al., 1982; Kehrl et al., 1985), no significant changes in pulmonary function or symptoms were detected in COPD patients in response to ozone exposure. In four of these five studies (Linn et al., 1982a; Linn et al., 1983; Solic et al., 1982; Kehrl et al., 1985), researchers studied patients with mild to moderate COPD who were exposed to 0.1 to 0.3 ppm ozone for 1 to 2-hours with intermittent light exercise with a $\underline{V}_E$ of 14 to 28 L/min. No consistent changes of arterial oxygen saturation were observed in these studies. However, based on the assumption that the response of pulmonary function to ozone may be a protective mechanism for the lungs from receiving more ozone in deep airways, failure of COPD patients to have pulmonary function responses to ozone might render these patients more susceptible to the pulmonary injury.

Very recently, Gong et al. (1997b) compared the responses to ozone exposure between COPD patients and the same age healthy subjects. Healthy subjects (60 to 69 years, n = 10) and subjects with severe COPD (59 to 71 years, n = 9) were exposed to air or 0.24 ppm ozone for 4-hours during intermittent light exercise ($\underline{V}_E$ 20 L/min). Symptoms, lung function, and arterial oxygen saturation were monitored. Overall COPD subjects had a 19% loss of FEV_1, while healthy subjects had a 2% loss ($p<0.001$). There were no significant changes in airway resistance in both groups following ozone exposure. Ozone exposure caused moderate changes in symptoms, and blood oxygenation in COPD patients, but not in healthy subjects. COPD patients appeared to be more sensitive to 0.24 ppm ozone-induced pulmonary function decrements and symptoms than healthy subjects.

Overall, more studies are required before a conclusion can be drawn regarding the susceptibility of COPD patients to ozone exposure.

Subjects with Asthma

In summary of the U.S. EPA criteria document (1996), studies by Linn et al. (1978), Silverman (1979), Koenig et al. (1985, 1987, 1988) have shown that no significant decrements in group pulmonary function could be elicited with ozone exposures ranging from 0.12 to 0.25 ppm for 40 minutes to 2-hours at rest or using light to moderate intermittent exercise ($\underline{V}_E$ 30 to 40 L/min) protocols in both adults and adolescents. Kreit et al. (1989) and Eschenbacher et al. (1989) used a heavy exercise protocol ($\underline{V}_E$ • 60 L/min) and ozone exposure at 0.40 ppm for 2-hours. Their data demonstrate that significant decreases in FVC, FEV_1, ratio of FEV_1 to FVC, and $FEF_{25\text{-}75\%}$ can be elicited in both normal and asthmatic subjects. Asthmatic patients were found to have greater decrements in all parameters except FVC and subjective symptoms when compared with normal subjects. Bronchial responsiveness as measured by the concentration of methacholine bronchoconstrictor required to increase 100% of airway resistance ($PC_{100SRaw}$) was also evaluated in these studies. While the asthmatic group had a lower baseline than the normal subjects, the percentage increase of bronchial responsiveness after ozone exposure was similar in normal and asthmatic subjects. These findings indicate that if the total inhaled dose (or effective dose) is increased significantly by either increasing $\underline{V}_E$ during exposure or ozone concentration, mild to moderate asthmatics will respond with a greater obstructive response than will normal subjects.

Using a prolonged exposure protocol, Linn et al. (1994) showed that exposure of asthmatic patients (18 to 50 years old, n = 30) to 0.12 ppm ozone for 6.5-hours with exercise ($\underline{V}_E$ 29 L/min), resulted in a statistically significant decrease in FEV_1. Exposure of healthy subjects (22 to 41 years old, n = 15) to the same protocol did not cause any spirometric changes. There was a greater but not statistically significant reduction in FEV_1 following ozone in asthmatics than in healthy subjects (-8.6% versus -1.7%).

Horstman et al. (1995) compared pulmonary function responses and symptoms of asthmatic (19 to 32 years old, n = 17) and non asthmatic (18 to 35 years old, n = 13) subjects to ozone. Subjects were exposed to 0.16 ppm ozone or air for 7.6-hours with intermittent light exercise ($\underline{V}_E$ 30 L/min). In this prolonged exposure study using low ozone concentration, asthmatic patients revealed significantly more decrements in FEV_1 and FEV_1/FVC than did healthy subjects. Nine of 17 asthmatics experienced wheezing with ozone, while no healthy subjects experienced wheezing. Six of 17 asthmatics requested inhaled β-agonist bronchodilator prior to and/or during ozone exposure and experienced some temporary alleviation of decrements. At the end of exposure, asthmatics who were medicated had greater ozone-induced decrements than those who were not medicated. Asthmatic subjects who had the larger ozone-induced FEV_1 decrements had lower baseline FEV_1/FVC and lower baseline % predicted FEV_1. It appears that in asthmatics, unlike non asthmatics, some portion of ozone-induced pulmonary function decrements experienced is related to bronchoconstriction, and that ozone-responsiveness for asthmatics depends upon baseline airway status.

J• rres et al. (1996) compared ozone-induced pulmonary function changes, symptoms and responsiveness to allergens among patients with mild stable allergic asthma (21 to 31 years old, n = 24), patients with allergic rhinitis without asthma (25 ± 3 years old, n = 12), and healthy subjects (23 ± 2 years old, n = 10). Subjects were exposed to filtered air or 0.25 ppm ozone for 3-hours during intermittent exercise ($\underline{V}_E$ 30 L/min). The concentration of methacholine ($PC_{20}FEV_1$) and the dose of allergen ($PD_{20}FEV_1$) producing a 20% fall in FEV_1 were determined. In asthmatic patients, FEV_1 decreased by 12.5 ± 2.2%, $PC_{20}FEV_1$ of methacholine by 0.9 ±• 0.19 doubling concentrations, and $PD_{20}FEV_1$ of allergen by 1.74 ±• 0.25 doubling doses, after ozone exposure. In the subjects with rhinitis, mean FEV_1 decrease was 14.1 ± 3.0% following ozone exposure. While allergen treatment worsened ozone-induced FEV_1 decrement, the responsiveness to methacholine was not altered by ozone exposure. In healthy subjects, mean FEV_1 decreased by 10.2 ±• 3.5% following ozone exposure. Allergen did not substantiate ozone-induced FEV_1 decrement in healthy subjects, and the responsiveness to methacholine was not altered by ozone exposure. There were no differences in ozone-induced symptoms among three groups. The data indicate that short term exposure to ozone can enhance bronchial responsiveness to inhaled allergens in asthmatic subjects, and likely in rhinitis subjects without asthma, but not in healthy subjects.

In the study conducted by McBride et al. (1994), researchers exposed 10 asthmatic subjects with histories of allergic rhinitis and 8 healthy subjects to 0, 0.12 and 0.24 ppm ozone for 90 minutes with light intermittent exercise ($\underline{V}_E$ 23 L/min). The authors did not find significant changes in pulmonary and nasal function in two groups of subjects. However, in asthmatic patients, a significant increase in the number of white blood cells in nasal lavage fluid was detected both immediately and 24 hours after exposure to 0.24 ppm ozone, as was a significant increase in epithelial cells immediately after exposure. A significant correlation was observed between interleukin-8 (IL-8) and white blood cell counts in the nasal lavage fluids after exposure to 0.24 ppm ozone ($r = 0.76$), although the levels of IL-8 were not significantly elevated after exposure to ozone. In healthy subjects, no significant changes in pulmonary or nasal function, or biochemical and cellular components were found in non asthmatics. The above studies suggest that asthmatic subjects have an exaggerated airway inflammatory response to acute ozone exposure, even when lung function is not affected.

However, in a study conducted by Hiltermann et al. (1995), data regarding ozone-induced hyperresponsiveness in asthmatic subjects are not quite consistent with reports by other groups. In this study, six asthmatic patients (22 to 27 years old) and 6 healthy subjects (20 to 40 years old) were exposed to air or 0.4 ppm ozone during 2-hours of exercise ($\underline{V}_E$ • 40 L/min). The authors found that FEV_1 dropped following ozone exposure to a similar extent in both asthmatic (15.3 ± 3.7%) and non-asthmatic (15.2 ± 4.0%) subjects. The percent changes of responsiveness to methacholine were significantly smaller in asthmatic subjects than in healthy subjects. However, asthmatic patients had higher baseline values for FEV_1 and responsiveness to methacholine challenge, indicating a pre-compromised physiological status. There was a significant rise in percent PMN in sputum in all subjects; however no correlation could be found between the changes in pulmonary function tests and those in cellular parameters. Since asthmatic patients have been 'pre-disposed' to a higher baseline value of responses, ozone exposure might facilitate the induction of an exacerbation of asthma, while the maximal plateau of responses induced by ozone may be independent of an underlying respiratory disease state.

Fernandes et al. (1994) investigated the effect of pre-exposure to 0.12 ppm ozone on exercise-induced asthma. Non smoking (26 ±• 7 years old, $n = 15$) subjects with mild stable asthma who had exhibited a fall in FEV_1 >15% after a standard 6 minute treadmill exercise challenge test were exposed to ozone or air for 1-hour at rest. The exposure was followed by a 6 minute exercise challenge; the treadmill speed and inclination were such that patients achieved their maximal exercise. The percent fall in FEV_1 and partial expiratory flow at 40% of vital capacity (V_{40p}) were not significantly different following exposure to ozone or air. The effects of exposure on the time course of spirometric responses after exercise showed no significant difference between air and ozone exposure. A study conducted by Weymer et al. (1994) comparing the responses of exercise-induced asthmatic versus non exercise-induced asthmatic patients to ozone reached a similar conclusion. In this study, of 21 asthmatic subjects, nine showed exercise-induced asthma positive, and 12 showed exercise-induced asthma negative. Subjects were exposed to 0, 0.1 or 0.25 ppm ozone for 1-hour with intermittent light exercise ($\underline{V}_E$ 27 L/min). Subjects then rested for 1-hour followed by a post exposure standardized exercise challenge in air. The researchers did not find significant changes in FEV_1 or FVC following 1-hour exposure to 0, 0.1 and 0.25 ppm ozone (regardless of exercise-induced asthma status). Increasing ozone concentration did not produce significant differences in FEV_1 response to post exposure exercise challenges for either the complete group or the subgroups with and without exercise-induced asthma. Thus, the researchers concluded that pre exposure to ozone does not sensitize the airways to subsequently produce greater exercise-induced airflow obstruction. Ozone-induced effects on airway mechanics are not additive or synergistic with exercise-related responses in asthmatics.

In summary, recent studies show that asthmatic subjects do not reveal substantially higher response in pulmonary function compared with healthy subjects when exposed to 0.12 to 0.4 ppm ozone for less than 3-hours. Pre-exposure to ozone (0.1 to 0.25 ppm for 1-hour at rest or with light exercise) does not aggravate exercise-induced asthma. However asthmatic subjects appear to have higher airway cellular responses (McBride et al., 1994) and higher responsiveness to allergens (Jörres et al., 1996; Hiltermann et al., 1995) than healthy subjects under these exposure conditions. With prolonged exposure (6.5 to 7.6-hours) to low concentrations of ozone (0.12 to 0.16 ppm) (Linn et al., 1994; Horstman et al., 1995), asthmatic subjects reveal higher pulmonary function response and symptoms than healthy subjects. These suggest that FEV_1 may not be a sensitive indicator for individual susceptibility to ozone insult. Because of the pre-existing compromised pulmonary function and an elevated value for bronchial responsiveness to methacholine in asthmatic patients compared with healthy people, ozone exposure might facilitate the induction of an exacerbation of asthma. The underlying mechanism that would explain a possible increased responsiveness of asthmatic subjects to ozone requires additional study.

Subjects with Allergic Rhinitis

Data on subjects with allergic rhinitis (inflammation of the nose or mucous membrane) and asthmatic subjects suggest that both of these groups have a greater rise in airway resistance to ozone (0.18 ppm for 2-hours with intermittent exercise) with a relative order of airway responsiveness to ozone being normal < allergic < asthmatic (McDonnell et al.,1987). Other early results have shown that in subjects with allergic rhinitis, acute exposure to ozone does not alter acute response to nasal challenge with antigen.

Jörres et al. (1996) investigated ozone-induced pulmonary function changes, symptoms and responsiveness to allergens in patients with mild stable allergic asthma (21 to 31 years old, n = 24), patients with allergic rhinitis without asthma (25 ± 3 years old, n = 12), and healthy subjects (23 ± 2 years old, n = 10). Subjects were exposed to filtered air or 0.25 ppm ozone for 3-hours during intermittent exercise ($\underline{V}_E$ = 30 L/min). The concentration of methacholine ($PC_{20}FEV_1$) and the dose of allergen ($PD_{20}FEV_1$) producing a 20% fall in FEV_1 were determined. In the subjects with allergic rhinitis, mean FEV_1 decrease following ozone exposure was equivalent to the FEV_1 decrements found in asthmatic patients. While allergen treatment worsened ozone-induced FEV_1 decrement, the responsiveness to methacholine was not altered by ozone exposure in rhinitis patients. In healthy subjects, mean FEV_1 decreased by 10.2 ± 3.5% following ozone exposure. Allergen did not substantiate ozone-induced FEV_1 decrement in healthy subjects, and the responsiveness to methacholine was not altered by ozone exposure. There were no differences in ozone-induced symptoms among the three groups. The data indicate that short term exposure to 0.25 ppm ozone can enhance bronchial responsiveness to inhaled allergens in allergic rhinitis subjects as well as in asthmatic subjects, but not in healthy subjects.

Subjects with Ischemic Heart Disease

Only one study has been reported in the U.S. EPA criteria document (1996) concerning the cardiopulmonary effects of acute ozone inhalation in patients with ischemic heart disease. Ischemic heart disease is caused by a deficiency of blood supply to the heart muscle due to obstruction or constriction of the coronary arteries. Six middle-aged male patients were exposed to air and 0.2 to 0.3 ppm ozone for 40 minutes with angina-symptom-limited exercise (mean $\underline{V}_E$ = 35 L/min). No significant pulmonary function impairment or evidence of cardiovascular strain induced by ozone inhalation was detected, but limitations in the study preclude any final conclusion.

In a study conducted by Drechsler-Parks (1995a), eight elderly healthy subjects (56 to 85 years of age) were exposed to either air or 0.45 ppm ozone, or 0.6 ppm nitrogen dioxide, or two pollutants in combination, for 90 minutes with intermittent exercise. Cardiac output was monitored by non-invasive impedance cardiography method, before and during the last 5 minutes of each exercise period. Exposure to ozone or nitrogen dioxide alone did not significantly modify cardiac output in comparison with air control. The exercise-induced increase in cardiac output was significantly smaller when subjects were exposed with nitrogen dioxide/ozone exposure than with air or ozone alone. The author speculates that the observed effects of nitrogen dioxide/ozone might be because nitrogen dioxide reacted with ozone and formed nitrate and nitrite, which might function as a vasodilator and subsequently caused a reduction of cardiac output.

Thus, due to the limited data reported, the responsiveness of subjects with ischemic heart disease to ozone exposure is inconclusive.

11.1.3 Influence of Gender, Age, Ethnic, and Environmental Factors

Gender Differences.

Based on the U.S. EPA criteria document (1996), the question as to whether there is a difference in responsiveness to ozone between men and women remains unresolved. Different conclusions can be drawn depending on whether $\underline{V}_E$ is normalized to body weight or lung size when the inhaled doses of ozone are calculated.

Frampton et al. (1997) exposed 56 never-smoking (age 25 ± 4 years, including 20 females) and 34 smoking (age 28 ± 1 years including 6 females) healthy subjects to 0.22 ppm ozone and air for 4-hours with exercise. By using multiple logistic regression analysis the authors found that gender, age and methacholine responsiveness were not predictive of responder status, although pack-year (annual consumption) of smoking was associated with decreased ozone responsiveness (OR = 0.87, p = 0.017).

Seal et al. (1996) investigated the effects of gender, age, socio-economic status and menstrual cycle phase on the pulmonary response to ozone exposure. Healthy African American and Caucasian subjects (18 to 35 years old, n = 372) were exposed once to air or 0.12, 0.18, 0.24, 0.3, or 0.4 ppm ozone for 2.3-hours with intermittent exercise ($\underline{V}_E$ • 45 - 55 L/min). Logistic function was used to model the exposure-response relationship, and the significant impact of gender, age, social economic status and menstrual cycle phase. While the researchers found that there were age and socio-economic effects on ozone-induced pulmonary function alterations, they did not find a significant gender effect, nor menstrual cycle effect, on individual sensitivity to ozone.

Data from a study conducted by Weinmann et al. (1995b) also show that there were no gender differences in pulmonary function responses to ozone. The authors exposed 24 healthy nonsmokers (12 men, age 27 ± 1 years; 12 women, age 25 ± 1 years) to 0.35 ppm ozone and air for 130 minutes with intermittent exercise ($\underline{V}_E$ 38 L/min). In order to detect the effects of ozone on small airway function, the researchers measured isovolumetric FEFs (forced expiratory flows), helium-oxygen (He-O_2), volume of isoflow (V_{isoV}), the multiple breath nitrogen washout (MBNW) curve, functional residual volume (FRC), and residual volume (RV) 24 hours after exposure. FEFs, He-O_2 and V_{isoV} were adjusted for any changes in FVC that occurred as a consequence of exposure, so that the pre and post exposure comparisons are isovolumetric and are designated as isoV. No gender differences in ozone responsiveness in small airway function were found, although isovolume (isoV) $FEF_{25\text{-}75}$, $Vmax_{50}$, $Vmax_{75}$ were reduced in all subjects combined at 25 minutes after ozone exposure, and showed no recovery at 24 hours.

Bush et al. (1996) studied the longitudinal distribution of ozone absorption in airways, and found that the absorption distribution of ozone in resting men and women was indistinguishable, although women absorbed ozone at smaller penetration volume than the men, and women had smaller dead space volume than the men. They concluded that previously reported gender differences may be due to a failure in properly accounting for tissue surface within the conducting airways.

Overall, the current literature does not suggest that there is a substantial gender difference in the responsiveness to ozone.

Hormonal Influences

Data reviewed in the U.S. EPA document (1996) did not permit any final conclusion on the influence of the menstrual cycle. The group sizes were again small for 2 (Fox et al., 1993; Gerbase et al., 1993) of the 3 studies and resulted in opposite conclusions. The third study (Seal et al.,1993a) compared race (African-American and Caucasian) and menstrual phase, obtaining a significant interaction between race and menstrual phase, but post hoc analysis failed to establish a basis for the interaction.

In a recent study by Seal et al. (1996), healthy women (18 to 35 years old, n = 150) were studied for the menstrual cycle effects on ozone-induced responses. The women were grouped into the appropriate menstrual cycle phase according to a menstrual history obtained immediately prior to ozone exposure. Subjects were exposed once to air or 0.12, 0.18, 0.24, 0.3, or 0.4 ppm ozone for 2.3-hours with intermittent exercise ($\underline{V}_E$ • 45 - 55 L/min). Logistic function analysis did not show any effects of menstrual cycle phase on ozone-induced pulmonary function responses.

Weinmann et al. (1995b) examined the effects of menstrual cycle phase on the responsiveness of small airway function parameters to ozone. Nine women were exposed to 0.35 ppm ozone for 130 minutes with intermittent exercise ($\underline{V}_E$ = 38 L/min), during the follicular and luteal phases. Ozone induced significant small airway dysfunction in all the subjects indicated by the reduction of isovolume FEF_{25-75}, $Vmax_{50}$, $Vmax_{75}$, as well as FVC and FEV_1. Neither the spirometric nor symptomatic responses differed significantly as a function of the menstrual cycle phase.

Age Differences

It has been hypothesized that age may be a factor in responsiveness to ozone. Few chamber studies exist on subjects under 18 (U.S. EPA, 1996), but field and epidemiology studies attempting to relate ambient air pollutant exposure to pulmonary function in children have suggested that children may be more responsive to ambient air pollution than young adults.

The response of adolescents and adults are not substantially different based on studies reported in the U.S. EPA document (1996). One of the problems that the authors noted seems to be the difficulty for children to perform consistent, reproducible pulmonary function tests.

Frampton et al. (1997) recently conduced exposure tests of healthy subjects (25 to 28 years of age, n = 90) to 0.22 ppm ozone or air for 4-hours with exercise ($\underline{V}_E$ for smokers and nonsmokers was 39 to 45 L/min and 43 to 46 L/min, respectively). Multiple logistic regression analysis did not show that age had any impact on individual pulmonary function responses to ozone exposure, although the amount of cigarette smoking was significantly associated with decreased ozone responsiveness (OR = 0.87). It should be noted that the narrow range of age in this study precludes any final conclusion on age effects.

Seal et al. (1996) exposed healthy African American and Caucasian subjects (18 to 35 years old, n = 372) once to air or 0.12, 0.18, 0.24, 0.3, or 0.4 ppm ozone for 2.3-hours with intermittent exercise ($\underline{V}_E$ • 45 - 55 L/min). Logistic function was used to model the exposure-response relationship, and the significant impact of age, social economic status and menstrual cycle phase. The ages of subjects within the studied range had an effect on sensitivity to ozone; younger subjects appear to be more responsive to ozone-induced decrements in FEV_1.

McDonnell et al. (1993) examined factors affecting ozone-induced FEV_1 decrements using a more homogeneous population, and found similar results. The authors exposed 290 white male subjects(18 to 32 years of age) to 0, 0.12, 0.18, 0.24, 0.3 or 0.4 ppm ozone for 2-hours with intermittent exercise ($\underline{V}_E$ • 70 L/min). Linear, quadratic, cubic and two sigmoid-shape models (the logistic and Gompertz functions) were used to describe decrements in FEV_1 as a function of ozone. Their model predicted a decreasing response with increasing age for all nonzero ozone concentrations. For exposure to 0.4 ppm, the model predicts decrements in FEV_1 of 1.07 and 0.47 L for 18 and 30 year old subjects, respectively. They concluded that for white males, age within the study range was significant predictor of response, with older subjects being less responsive to ozone.

The available data in the U.S. EPA document (1996) indicate that responsiveness to ozone is decreased in persons over 50 years of age compared to young adults. Recently Drechsler-Parks (1995b) investigated pulmonary function responses in 9 male healthy elderly subjects (56 to 71 years) following exposure to air and 0.45 ppm ozone for 2-hours. Exposure concentrations of ozone were altered by varying $\underline{V}_E$ through exercise. At $\underline{V}_E$ of 25, 40 and 55 L/min, ozone exposure induced small, significant decrements in FVC (-5.31%, -6.47% and -5.29%, respectively) and FEV_1 (-7.54%, -7.59% and -10.43%, respectively), but no significant changes in $FEF_{25\text{-}75\%}$. There were no significant differences among responses to the three ozone exposures. When taking into account the effective dose of ozone (concentration x $\underline{V}_E$ x duration), ozone-induced decrements of pulmonary function in older subjects were much smaller than those typically observed in young males exposed to similar inhaled doses of ozone.

More recently, Gong et al. (1997b) studied the effects of ozone on elderly healthy subjects (60 to 69 years, n = 10) and subjects with severe COPD (59 to 71 years, n = 9). Subjects were exposed to air or 0.24 ppm ozone for 4-hours during intermittent exercise ($\underline{V}_E$ = 20 - 30 L/min). Symptoms, lung function, and arterial oxygen saturation were monitored. While COPD subjects had 19% loss of FEV_1, healthy subjects had only 2% loss of FEV_1. There were no significant changes in airway resistance in both groups following ozone exposure. Ozone exposure did not cause changes in symptoms, and blood oxygenation in healthy subjects. Four-hour exposure to 0.22 ppm ozone has been shown to initiate >15% of decrements in FEV_1 in young healthy subjects with moderate exercise ($\underline{V}_E$ • 40 - 46 L/min) (Torres et al., 1996; Frampton et al., 1997). Thus, overall elderly subjects are revealed to be less sensitive to ozone-induced pulmonary function decrements and symptoms than young healthy subjects.

Ethnic and Racial Factors

Only one study (Seal et al., 1993b) has been conducted to investigate these potential factors in the U.S. EPA document (1996). Although 372 subjects (approximately 90/sex/race—African American & Caucasian), each subject only participated in one experimental session (6 dose groups ranging from 0.00 to 0.40 ppm ozone). A multiple comparison analysis was used to identify specific differences among the gender-race groups when an overall group effect was detected. African American males experienced significant decrements in FEV_1 following exposure to 0.120 ppm of ozone, whereas black women and white men and women did not have significant decrements in FEV_1 at ozone concentrations below 0.180 ppm. The results are suggestive of an ethnic difference, but more subjects must be studied before a final conclusion can be reached.

In recent years, no new studies have been reported regarding the race effects on ozone responsiveness.

Environmental Factors

A number of environmental factors, such as ambient temperature and humidity, season of the year, route of inhalation, and smoking history have been hypothesized to potentially impact on responses to ozone exposure in additive or synergistic ways. To date, none of these factors have been studied adequately to reach final conclusions. The few studies performed to examine the effects of temperature and humidity produced, at best, equivocal results.

The issue of nasal versus oral inhalation of ozone has been studied to some extent. This issue is important since chamber studies have been performed with subjects breathing freely while others used mouthpiece exposure systems. The results from the studies by Hynes et al. (1988) and

Adams et al. (1989) would tend to demonstrate that there is no difference in pulmonary function regardless of the route of inhalation exposure.

Two studies reported in the U.S. EPA document (1996) demonstrated that current smoking may blunt responsiveness to ozone exposure (Emmons & Foster, 1991) and that smoking cessation for 6 months leads to improved baseline pulmonary function and possibly the re-emergence of ozone responsiveness (Frampton et al., 1993).

Data published recently by Frampton et al. (1997) support these observations. In this study, 56 never-smoking (age 25 ± 4 years) and 34 smoking (age 28 ± 1 years) healthy subjects were exposed to 0.22 ppm ozone and air for 4-hours with exercise ($\underline{V}_E$ for smokers and nonsmokers was 43 to 46 L/min and 39 to 45 L/min, respectively). Multiple logistic regression analysis reveals pack-year of smoking to be associated with decreased ozone responsiveness (OR = 0.87, p = 0.017); healthy smokers had smaller decrements of FEV_1 in response to ozone exposure than did nonsmokers. Smokers reported fewer respiratory symptoms than did nonsmokers following ozone exposure, but the difference was significant only for cough. The researchers speculate that the decreased responsiveness of smokers to ozone might be because the oxidative chemicals in cigarette smoke attenuated irritant-receptor responsiveness and increased the mucous layer lining the airways in smokers.

11.1.4 Co-pollutants

Ambient air pollution is composed of a complex mixture of gases and particles, and therefore potential interactions among various pollutants should be taken into consideration.

The U.S. EPA criteria document (1996) reviewed the evidence for the interactions between ozone and co-pollutants, and concluded that no significant enhancement of respiratory effects (more than additive) in healthy subjects has been consistently demonstrated for mixtures of ozone (0.12 to 0.16 ppm, 1 to 2-hours) with ambient concentrations of SO_2, NO_2, H_2SO_4, HNO_3, and peroxyacetyl nitrate (PAN). At higher concentrations, PAN (0.30 ppm) combined with ozone exposure (2-hours) has resulted in greater pulmonary function responses than ozone (0.485 ppm) alone in healthy subjects (Horvath et al., 1986).

In asthmatic adolescents, pre exposure to ozone (0.12 ppm, 45 minutes, $\underline{V}_E$ = 30 L/min) followed by low level of SO_2 (0.1 ppm, 15 minutes) elicited a greater degree of bronchial responsiveness than did pure air followed by SO_2 or by two exposures to ozone alone, indicating some synergism between the effects of SO_2 and ozone (Koenig et al.1990). Both ozone and SO_2 concentrations were at subthreshold levels for the experimental design used.

Recent studies support the previous observations. Frampton et al. (1995) evaluated symptoms and pulmonary function responses of 30 healthy (28 ± 5 years old) and 30 allergic asthmatic (28 ±• 7 years old) subjects to sulphuric acid aerosol and ozone. Each subject was studied 4 times, receiving 100 $\mu g/m^3$ sulphuric acid (MMAD [mass median average diameter] 0.66 μm) or NaCl aerosols (MMAD 0.45 μm), for 3-hours as pre-exposure. One day later (24 hours), the subject was exposed to 0.08, 0.12, or 0.18 ppm ozone for 3-hours. During each exposure, subjects performed intermittent exercise ($\underline{V}_E$ 33 to 40 L/min). In healthy subjects, there was no convincing evidence for a symptomatic or physiologic effect of exposure to either NaCl or sulphuric acid aerosols or ozone alone, and there was no clear evidence for an effect of aerosol pre-exposure on the ozone response. In asthmatic patients, ozone (starting from 0.08 ppm), NaCl and sulphuric acid aerosols independently caused decrements of FVC and FEV_1. Sulphuric acid aerosol altered the pattern of spirometric response to ozone in comparison with NaCl pre-exposure and appeared to enhance the small mean decrements in FVC and FEV_1 that occurred in response to 0.18 ppm ozone. Individual responses among asthmatics varied markedly, some demonstrating reductions in FEV_1 of more than 35% following ozone exposure.

Pre exposure of healthy subjects (18 to 35 years old, n = 21) to NO_2 followed by ozone has shown to enhance ozone-induced spirometric changes (Hazucha et al., 1994). Subjects were exposed to 0.6 ppm NO_2 or air for 2-hours, and 3-hours later exposed to 0.3 ppm ozone for 2-hours. Subjects performed intermittent exercise ($\underline{V}_E$ • 40 L/min). NO_2 alone did not reduce FEV_1, but did significantly enhance ozone-induced spirometric changes. No significant effects were observed in airway resistance. Following the NO_2/ozone exposure, the median bronchial responsiveness to methacholine was significantly reduced compared with the air/ozone exposure.

Utell et al. (1994) studied the effect of pre exposure to acid aerosols on ozone-induced pulmonary function and symptoms. Healthy (18 to 45 years, n = 30) and asthmatic (18 to 45 years, n = 30) nonsmoking subjects were exposed to particulate aerosols (sulphuric acid 100 $\mu g/m^3$ or NaCl 100 $\mu g/m^3$) for 3-hours. Twenty-four hours later, subjects were exposed to ozone (0.08, 0.12 and 0.18 ppm) for 3-hours. Intermittent exercise was performed during both exposures ($\underline{V}_E$ for healthy subjects was 40 L/min, for asthmatics was 30 to 36 L/min). In healthy subjects, no lung function changes or symptoms were seen in either aerosol or ozone exposures. No interaction of either particle with ozone was found in healthy subjects. In asthmatic subjects, pre exposure to sulphuric acid had no direct effect on lung function but appeared to enhance the small mean decrements in FVC that occurred in response to 0.18 ppm ozone. Therefore, exposure to ozone and other pollutants in a sequential fashion seems to reveal a synergistic effect on ozone-induced spirometric responses.

Linn et al. (1995) exposed asthmatic children (11 to 18 years, n = 24) to clean air, or 0.2 ppm ozone + 0.3 ppm NO_2, or ozone + NO_2 + sulphuric acid aerosol (MMAD 0.66 μm, concentration equivalent to 127 $\mu g/m^3$ sulphuric acid) with intermittent exercise ($\underline{V}_E$ = 32 L/min) for 90 minutes. Subjects gargled lemonade to minimize acid neutralization by oral ammonia. Differences in group mean FEV_1 among ozone/NO_2/acid aerosol, ozone/NO_2 and air exposures were not significant. An earlier study conducted by the same research group (Linn et al., 1994) has shown that repeated, multi-hour exposure of healthy and asthmatic adults to a low level of ozone (0.12 ppm with exercise $\underline{V}_E$ at 29 L/min) plus sulphuric acid aerosol (100 $\mu g/m^3$ respirable acid aerosol, MMAD 0.5 μm) did not cause substantially higher spirometric and symptomatic changes than exposure to ozone alone. However both asthmatic and healthy subjects showed substantial diversity with respect to the individual responsiveness to the combined exposure.

In addition to pulmonary function, Aris et al. (1993) also examined airway inflammatory responses in 10 healthy subjects following exposure to 500 μg/m^3 of HNO_3 alone, or HNO_3 + 0.2 ppm ozone, or ozone alone, for 4-hours. During exposure, subjects performed intermittent exercise (40 L/min). BAL, PAL (proximal airway lavage) and bronchial biopsy (to see proximal airway injury) were performed 18 hours after exposure. While exposures to HNO_3/ozone and ozone alone were associated with significant decrements in FEV_1 and FVC and increases in airway resistance, and increases of neutrophils, proteins, albumin, fibronectin, and α1-antitrypsin in BAL; there were no significant differences in these endpoints between the HNO_3/ozone and ozone exposure. There were no differences in pulmonary function parameters or in the cellular or biochemical constituents in either BAL or the PAL between HNO_3 and air exposure. There were no significant differences in the bronchial biopsy specimens between the HNO_3 and air exposures, or between the HNO_3/ozone and ozone exposures. Thus, the data do not suggest that HNO_3 gas causes either proximal airway or distal lung injury or that HNO_3 potentiates the inflammatory response produced by ozone in healthy individuals.

The assessment of such mixtures is, therefore, far from complete and much work needs to be done. Few studies have included more than two chemicals, and the endpoints measured are often limited to pulmonary function variables.

11.1.5 Repeated Exposures to Ozone

A repeated exposure study is designed to determine health effects after several consecutive days of exposure to ozone. As summarized in the U.S. EPA document (1996), the spirometric responses to repeated ozone exposure typically show that the response is increased on the second exposure day to concentrations in the range of 0.40 to 0.50 ppm ozone in exposures accompanied by moderate exercise. This phenomenon was not observed at lower concentrations or in groups with relatively small ozone-induced decrements in spirometry.

Two studies (Bedi et al., 1985; Folinsbee et al., 1986) indicated that enhanced spirometric responsiveness was present within 12 hours after exposure to ozone (0.25 to 0.45 ppm for 1 to 2-hours), and lasted for at least 24, and possibly 48, hours, but was clearly absent after 72 hours. After 3 to 5 days of consecutive daily exposure to ozone, responses were markedly diminished or absent. Horvath et al. (1981) had previously observed similar attenuation of lung function decrements following repeated exposure to 0.42 ppm ozone for 5 consecutive days. The authors suggested that the rapidity of this decline in response was related to the magnitude of the subjects' initial responses to ozone or their sensitivity.

Other observations by Gliner et al. (1983) and Brookes et al. (1989) suggest that although pre exposure to low concentrations of ozone (0.2 ppm) may not influence response to higher concentrations, pre exposure to a high concentration of ozone (0.35 ppm) may significantly increase response to a lower concentration (0.2 ppm) the following day.

Schonfeld et al. (1989) also showed that the responses to a second exposure (0.35 ppm ozone) were clearly increased at 24 hours and possibly at 48 hours, but with a 3 or 4 day interval, the responses were similar. The persistence of the attenuation of spirometric and symptom responses is relatively short-lived, being partially reversed within 3 to 7 days and typically abolished within 1 to 2 weeks. Linn et al. (1982b) have shown that repeated exposure (0.47 ppm ozone) separated by a week for up to 6 weeks did not cause any lessening of the spirometric response.

Repeated prolonged (6 to 7-hours) exposure to low concentrations of ozone has also been examined (Horvath et al., 1991; Linn et al., 1991, 1992). The results appear to show an attenuation of symptoms and pulmonary function changes with repeated exposure to low levels of ozone. Folinsbee et al. (1994) recently exposed 17 healthy adults (25 ± 4 years of age) to 0.12 ppm ozone for 6.6-hours/day for 5 consecutive days, using an intermittent exercise protocol ($\underline{V}_E$ = 39 L/min). FEV_1 changes averaged -12.79, -8.73, -2.54, -0.6, and +0.18% on the 5 exposure days. Airway responsiveness to methacholine challenge was significantly increased after each ozone exposure. The mean ratios were 2.00, 3.67, 4.55, 3.99, 3.24, and 3.74 for air and ozone days 1 to 5, respectively. Respiratory symptoms increased significantly on ozone day 1 only. Thus, repeated prolonged exposure to low levels of ozone results in progressive but transient attenuation of pulmonary function responses.

In a very recent study conducted by Gong et al. (1997a), mild asthmatic subjects (20 to 48 years old, n = 10) were exposed to 0.4 ppm ozone, 3-hours/day for 5 days, with intermittent exercise ($\underline{V}$= 32 L/min). Follow-up exposures to 0.4 ppm ozone were performed 4 and 7 days after the most recent consecutive exposure to study the tolerance to ozone. Symptoms and decrements of FEV_1 (-35% on day 1, and -34% on day 2) progressively diminished after the third day exposure, with only 6% decrement of FEV_1 on day 5. The tolerance was partially lost 4 and 7 days later, with mean FEV_1 losses of 15% and 17% respectively. Bronchial reactivity to methacholine peaked after the first ozone exposure, and remained elevated after all subsequent ozone exposures relative to the levels in air control. The data indicate that asthmatics can develop tolerance to high level ozone in a similar pattern as normal subjects.

Linn et al. compared healthy subjects versus asthmatics in their adaptation to repeated ozone exposure (Linn et al., 1994). Healthy (22 to 41 years, n = 15) and asthmatic (18 to 50 years, n = 30) subjects were exposed to filtered air, 0.12 ppm ozone, ozone + 100 $\mu g/m^3$ respirable sulphuric acid aerosol (MMAD 0.5 μm), or acid aerosol alone, with six 50-minute exercise periods (29 L/min), total 6.5-hours/day for 2 days. Exposure to ozone alone or ozone plus acid aerosol caused a progressive, significant decline in FEV_1 and a progressive increase in airway resistance, smaller on the second day than the first day in both asthmatic and healthy subjects. Bronchial reactivity to methacholine challenge increased significantly after exposure to ozone with or without acid aerosol on the first day, and declined after the second day exposure. Changes in mean lung function and bronchial reactivity with ozone plus acid exposure were modestly but not significantly larger than changes with ozone alone. A minority of asthmatics and non asthmatics showed substantially greater declines in function with exposure to ozone plus acid relative to ozone alone. Overall ozone-induced changes of FEV_1 and bronchial responsiveness in healthy and asthmatic subjects were attenuated to a similar extent; however asthmatics were more sensitive to ozone or ozone plus acid than healthy subjects.

The U.S. EPA criteria document (1996) summarized a series of studies from the Rancho Los Amigos group. The studies were designed to examine changes in the spirometric and symptomatic responses to ozone in a year including the 'smog season' in the Los Angeles/South Coast Air Basin. The results suggest a seasonal variation in physiological responses that may be attributed to increased ambient ozone exposure during the summer months. In agreement with the findings from repeated ozone exposure studies, 'responders' became less responsive to 0.18 ppm ozone after 'smog season'. However, 'responders' included subjects who had a history of complaints from ambient air pollution. The group also included a significant proportion of allergic individuals, which may have contributed to their varying responses. Historically, studies with subjects from L.A. have reported reduced responses to ozone in the laboratory compared to non-residents (Hackney et al., 1976, 1977).

Besides the absence of pulmonary function responses after repeated ozone exposure, a study by Devlin et al. (1997) has demonstrated that airway inflammatory responses are also attenuated. In this study, healthy young nonsmoking male subjects (20 to 48 years old, n = 16) were exposure to 0.4 ppm ozone, 2-hours/day for 5 days, with intermittent exercise ($\underline{V}$= 60 L/min). Follow-up exposures to 0.4 ppm ozone were performed 10 (9 subjects) or 20 (7 subjects) days after the last exposure day. Bronchoalveolar lavage was performed after 5 days of exposure to ozone and air, and a third time after the 10 or 20 day follow-up ozone exposure. Cell differential, interleukin-6, (IL-6) IL-8, PGE_2, elastase, fibronectin, protein, α1-antitrypsin, lactate dehydrogenase (LDH), were determined in BAL. Alveolar macrophage phagocytosis of yeast was also measured. Their data demonstrate that after 5 days of exposure, ozone-induced increases in percent PMN, IL-6, prostaglandin E_2, elastase and fibronectin were diminished. Ozone-induced decreases in recovery of viable BAL cells and alveolar macrophage phagocytosis of yeast were blunted. Within 10 to 20 days, percent PMN, IL-6, PGE_2, fibronectin, and recovery of viable cells showed at least partial reversal, while other mediators did not return to the normal response to ozone. It is concluded that biochemical mediators in response to ozone were attenuated after 5 consecutive days of ozone exposure. However, markers of cell injury were not attenuated and may indicate a persistent but not perceived effect of ozone. Inflammatory responses could be invoked to explain at least a portion of the pulmonary function responses.

Airway responsiveness to methacholine is increased with an initial ozone exposure (Holtzman et al., 1979; Folinsbee et al., 1988; Folinsbee et al., 1994; Gong et al., 1997a). One interesting finding is that at low (0.12 ppm) or high (0.4 ppm) concentrations of ozone, responsiveness to methacholine was increased over the 5 days of multi-hour exposure period when compared to air control (Folinsbee et al., 1994; Gong et al., 1997a). However, Kulle et al. (1982) and Dimeo et al. (1981) reported a tendency for the increased responsiveness to diminish with repeated exposure to ozone.

Overall, several conclusions can be drawn about repeated exposure to ozone:

1. Repeated exposure to high concentrations of ozone (0.35 to 0.45 ppm) for 1 to 2-hours can cause an enhanced spirometric response on the second day of exposure. This enhancement appears to be dependent on the interval between the exposures, with 24

hours causing the greatest increase, and absent with intervals ≥ 3 days. An enhanced response also appears to depend to some extent upon the magnitude of the initial response. Small responses to the first ozone exposure are less likely to result in an enhanced response on the second day of ozone exposure.

2. Repeated daily exposure also results in attenuation of spirometric responses, typically after 3 to 5 days of exposure. This attenuation may persist for less than 1 or 2 weeks. In temporal conjunction with the spirometry changes, symptoms induced by ozone, such as cough and chest discomfort are also attenuated with repeated exposure.

3. Ozone-induced changes in airway responsiveness to methacholine attenuate somewhat more slowly than do spirometric and symptom responses. Attenuation of the changes in airway responsiveness may also persist longer than changes in spirometry, although this has only been studied on a limited basis.

4. Exposures at lower concentration for longer duration do not cause an enhanced second-day response. The attenuation of response to ozone appears to proceed more rapidly.

5. Asthmatics can develop tolerance to high level ozone in a similar fashion as normal subjects. When compared with healthy subjects, asthmatics appear to be more sensitive to repeated exposure to ozone than healthy subjects.

6. Limited studies on BAL have also shown that several inflammatory markers may be attenuated following repeated exposure to ozone. This may impair the host defense system, and render subjects susceptible to infectious diseases.

11.1.6 Effects on Exercise Performance

An early epidemiological study examining race performances in high school cross-country runners (Wayne et al., 1967) suggested that exercise performance is depressed by inhalation of ambient oxidant air pollutants. Controlled human studies regarding the effects of ozone inhalation on exercise performance can be divided into two categories, those that examine the effects of acute ozone inhalation on maximal oxygen uptake ($\underline{V}O_{2max}$), and those that examine the effects of acute ozone inhalation on subjects' ability to complete strenuous continuous exercise protocols up to 1-hour in duration.

Effects on Maximal Oxygen Uptake ($\underline{V}O_{2max}$)

To summarize studies reviewed by the U.S. EPA document (1996), when the exercise is preceded by an ozone exposure entailing a sufficient total inhaled dose of ozone to result in significant pulmonary function decrements and/or subjective symptoms of respiratory discomfort, maximal oxygen uptake appears to be reduced. Simply stated, the effective dose is what counts. Exposure to ozone at a concentration of 0.75 ppm for 2-hours with intermittent exercise can result in reductions of $\underline{V}O_{2max}$, maximum ventilation, maximum attained workload, and maximum heart rate

(Folinsbee et al. 1977), whereas the same concentration at rest did not induce any effects except a significantly decreased FVC (Horvath et al., 1979). Other studies have confirmed these findings.

Effects on Endurance Exercise Performance

This effect is more subjectively assessed. Many investigators cited in the U.S. EPA document (1996) have concluded that the observed reductions in exercise performance appear to be due to symptoms limiting the ability of the subjects to perform. However, in every case, this conclusion is reached by exclusion and not by a demonstration of causal relationship.

Ozone concentrations as low as 0.06 ppm have been reported to cause small decrements in performance time during a progressive maximal exercise test (at $\underline{V}_E$ of 30 to 120 L/min for 16 to 28 min) (Linder et al., 1988). Avol et al. (1984a) reported that 3 out of 5 well-conditioned cyclists could not complete the 1-hour exposure to 0.16 ppm ozone, without a reduction in workload.

One hypothesis proposed for ozone-induced reduction of exercise performance is that the stimulation of neural receptors in the airways by ozone may result in an inhibition of α-motor nerve activity to respiratory muscles during inspiration (Koepchen et al., 1977; Schmidt and Wellhoner, 1970). This may result in the observed decrease in V_T (U.S. EPA, 1996), while at the same time increasing the subjects' sensation of respiratory effort. A reflex inhibition of the ability to inspire would be consistent with the reduced V_T following ozone exposure in subjects performing maximal exercise, and would be consistent with the development of a physiologically induced ventilatory limitation to maximal oxygen uptake.

11.2 PULMONARY FUNCTION EFFECTS OF PROLONGED (MULTI-HOUR) OZONE EXPOSURES

A series of studies has described the responses of healthy and asthmatic subjects exposed to relatively low ozone concentrations for durations of 4 to 8 hours. These studies have demonstrated statistically significant changes in lung function, symptoms and airway responsiveness during and after exposures. Unlike repeated-exposure studies, prolonged exposure studies demonstrated lung function decrements in a concentration-dependent fashion, and did not show an attenuation at the end of the exposure.

Two primary studies are described in the U.S. EPA document. The first one, conducted by Folinsbee et al. (1988), utilized an 'EPA prolonged-exposure protocol'. In order to simulate heavy outdoor work or play, healthy nonsmoking male subjects (18 to 33 years, n = 10) exercised at a moderate level ($\underline{V}_E$ at 40 L/min for 50 minutes and 10 minutes rest) for 3-hours, then had a 35 minute (0.6-hour) lunch break (with continuous exposure to ozone at rest) followed by another 3-hours of intermittent exercise. Total exposure time was 6.6-hours. During the intermittent exercise, subjects were exposed to 0.12 ppm ozone. FVC and FEV_1 decreased in a time-dependent pattern during the exposure. Increased symptoms were observed and airway responsiveness to methacholine was approximately doubled after ozone exposure. Likewise, Horstman et al. (1990) adapted the same exercise protocol to expose 22 healthy nonsmoking male subjects (18 to 33 years of age, n = 22) to clean air and 0.08, 0.10, and 0.12 ppm of ozone, and found a similar response pattern. The decrements of FEV_1 were ozone concentration-dependent, with a concentration as low as 0.08 ppm causing a 7% reduction of FEV_1.

Larsen et al. (1991) applied that information (Horstman et al., 1990) to a lognormal multiple linear regression model to develop a dose—response relationship for percent changes in FEV_1 as a function of ozone concentration and exposure duration. The results suggest that FEV_1 responses were approximately linear with duration of exposure but that ozone concentration plays a more important role. The exponent of approximately 4/3 suggests that doubling ozone concentration would be similar to increasing exposure duration by about 2.5 times (see Figures 11.1 and 11.2).

Other studies such as that conducted by McDonnell et al. (1991a) have assisted in confirming the above findings. The duration-FEV_1 response data were fit to a three parameter logistic model, which significantly improved the amount of variance explained by the model compared to the linear model. The reasonably good fit to the logistic model suggests that the ozone-pulmonary function response relationship may have a sigmoid shape. The main importance of this observation is that it suggests a response plateau. That is, there is a level of response (i.e., plateau) to a given ozone concentration and exercise ventilation level (i.e., dose rate) beyond which decrements in FEV_1 response tend not to increase with increasing duration of exposure.

Folinsbee et al. (1991) utilized the data from 4 different studies conducted at the U .S. EPA Health Effects Research Laboratory using the U.S. EPA prolonged-exposure protocol, and examined the distribution of responses among subjects at 3 different concentrations. Decrements in FEV_1 as large as 30 to 50% were observed with prolonged exposure to 0.12 ppm of ozone or less. In fact, with respect to the distribution, it is noted that none of the subjects showed a drop of >10% in the clean air group, whereas in the 0.08, 0.10, and 0.12 ppm groups, 26, 31, and 46% of the subjects had >10% decrements in FEV_1, respectively. This serves to illustrate the variability of responses under similar exposure conditions.

Figure 11.1 Ozone dose-response curves of FEV1 lung function decrease—fitted using the lognormal distribution (from Larsen et al., 1991)

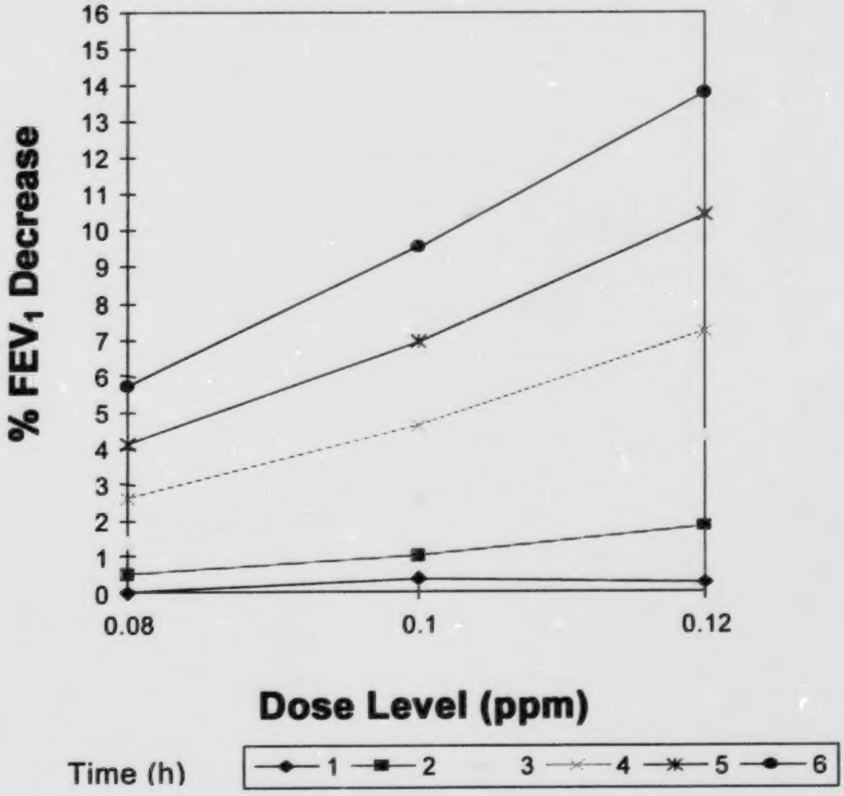
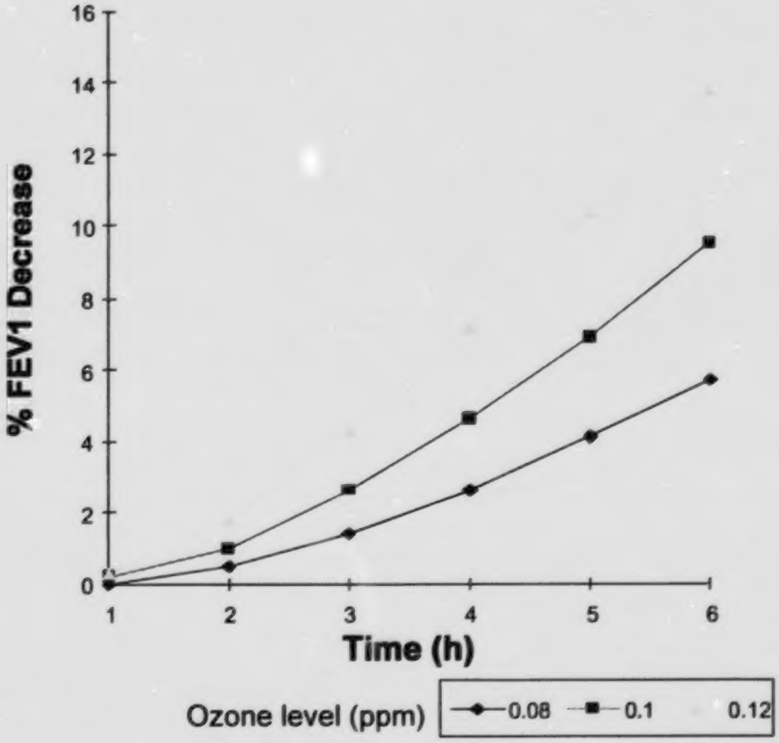


Figure 11.2 Decrease of FEV1 over time. (Lognormal values, from Larsen et al., 1991)



Hazucha et al. (1992) designed a protocol to examine the effect of varying, rather than constant, ozone concentration. In the study, male subjects (20 to 35 years old, n = 23) were exposed to filtered air, a constant concentration of 0.12 ppm ozone, or a linearly variable concentration of ozone ranging from 0 at the start to 0.24 ppm at 4-hours and back down to 0 ppm at 8-hours (end of experiment). Subjects performed intermittent exercise ($\underline{V}_E$ at 40 L/min). No effects were noted in the filtered air group. At a constant 0.12 ppm of ozone, FEV_1 was decreased by 5% at the fifth hour. In the variable concentration group, the FEV_1 decreased almost twice of that in the constant concentration group after 6 hours of exposure. FEV_1 began to improve and was reduced by 5.9% at the end of the 8-hour exposure. This study illustrates two important points for those modelling spirometric responses to ozone exposure. First, the model should include a response plateau and secondly, the response to ozone exposure is dependent on the dose rate as well as the cumulative dose, at least when the ozone concentration is varied.

More recently, several studies have been carried out using an exercise protocol similar to the 'EPA prolonged exposure protocol' (Basha et al., 1994; Folinsbee et al., 1994; McDonnell et al., 1995; Horstman et al., 1995), in order to investigate the effects of 6- to 8-hour exposure to ozone (0.08 to 0.2 ppm, with exercise at $\underline{V}_E$ of 30 - 40 L/min). The findings of spirometric and symptomatic responses were consistent with the previous reports (Folinsbee et al., 1988, Horstman et al., 1990). Healthy subjects (18 to 45 years old) experienced significant time-dependent and ozone concentration-dependent loss of FEV_1, at a concentration as low as 0.08 ppm (McDonnell et al., 1995). In the case of asthmatic patients (18 to 50 years old), most studies show that decrements in FEV_1 for asthmatics were significantly greater than for non asthmatics (Linn et al., 1994; Horstman et al., 1995). However one study conducted by Basha et al. (1994) demonstrates that asthmatic subjects were no more responsive to a 6-hour exposure of 0.2 ppm ozone than their healthy counterparts in pulmonary function decrements, although cellular and biochemical inflammatory parameters in BAL were more augmented in asthmatic subjects than in healthy ones.

In general, data from prolonged ozone exposure studies further confirm the essential concept of the 'effective dose', namely, ozone concentration x ventilation rate x exposure duration, although ozone concentration apparently contributes more to pulmonary responses than does ventilation or exposure duration. More importantly, on the grounds of the 'effective dose', there appears not to exist a lower threshold for ozone-induced spirometric responses; a prolonged ozone exposure at a concentration of $\leq$0.08 ppm (the current National Ambient Air Quality Objective for ozone) may still exhibit an adverse health effect.

11.3 INCREASED AIRWAY RESPONSIVENESS

Increased airway responsiveness is an important consequence of exposure to ozone. An elevated airway responsiveness to methacholine challenge indicates that the airways are predisposed to bronchoconstriction induced by a variety of stimuli (e.g., specific allergens, sulphur dioxide, cold air, etc.). The dose of a bronchoconstrictor (such as methacholine and histamine) that causes a 20% drop in FEV_1 or a 100% increase in airway resistance is referred to as the PD_{20} or the PD_{100} respectively.

A high level of bronchial responsiveness is a hallmark of asthma. Historically, the range of nonspecific responsiveness (expressed as PD_{20}) between the least sensitive healthy subject and the most sensitive asthmatic is about 1000 fold. All other types of 'responders' (e.g., atopic or allergic individuals) would fall between these values. The average changes in airway responsiveness induced by ozone range from 150 to 500% (U.S. EPA criteria document, 1996). This suggests that a healthy subject could move from the normal range to the mild asthmatic range of airway responsiveness when exposed to ozone.

Data summarized in the U.S. EPA document (1996) suggest that ozone-induced increases in airway responsiveness usually resolve 18 to 24 hours after exposure (Holtzman et al., 1979; Folinsbee & Hazucha, 1989; K• nig et al., 1980), while the hyperresponsiveness may persist in some individuals for longer periods (Golden et al., 1978). Increased airway responsiveness to histamine and methacholine has been observed following exposure to 0.20 ppm ozone for 1-hour (vigorous exercise) (Gong et al., 1986), and 0.08 to 0.12 ppm ozone for 6.6-hours with intermittent exercise ($\underline{V}_E$ at 39 - 50 L/min) (Folinsbee et al., 1988; Horstman et al., 1990).

Data from the latest studies further demonstrate that 0.24 ppm ozone (4-hours with exercise at $\underline{V}_E$ of 20 L/min) did not cause a significant increase in bronchial reactivity in response to methacholine challenge in elderly healthy subjects (60 to 69 years) (Gong et al., 1997b). Based on the effective dose, elderly subjects appear to be less sensitive to ozone-induced airway hyperresponsiveness in comparison with young people. In allergic asthmatic subjects (21 to 31 years old), a 3-hour exposure to 0.25 ppm ozone ($\underline{V}_E$ at 30 L/min) initiated significant increases in bronchial responsiveness to methacholine and allergen (J• rres et al., 1996). No alteration in bronchial responsiveness to methacholine was observed in healthy subjects and subjects with allergic rhinitis without asthma, although subjects with allergic rhinitis did show a bronchial allergen response after ozone exposure (J• rres et al., 1996). While an 1-hour exposure to 0.12 ppm ozone at rest did not cause an increased responsiveness to methacholine challenge in asthmatic patients (Ball et al., 1996), prolonged exposure (6.6-hours) to this concentration with exercise ($\underline{V}_E$ at 29 L/min) did induce an enhanced bronchial reactivity in asthmatics (Linn et al., 1994).

Publications on 'adaptation' or tolerance, of increased bronchial responsiveness to methacholine challenge following repeated exposure to ozone are not consistent. Data from two early studies (Kulle et al., 1982, Dimeo et al., 1981) exhibit a trend to the increased responsiveness to diminish with repeated exposure to ozone, starting on or after the third day of consecutive exposure. However, two later studies demonstrate that at low (0.12 ppm, 6.6-hours/day, $\underline{V}_E$ at 39 L/min) (Folinsbee et al., 1994) and high (0.4 ppm, 3-hours/day, $\underline{V}_E$ at 32 L/min) (Gong et al., 1997a) concentrations of ozone, bronchial responsiveness to methacholine remained elevated over the 5 days of multi-hour exposure period in both healthy (n = 17) (Folinsbee et al., 1994) and asthmatic (n = 10) (Gong et al., 1997a) subjects.

There is no doubt that ozone produces acute increases in airway responsiveness. However, it is not known if ozone exposure causes protracted increases in airway responsiveness in healthy individuals, or even induces or predisposes subjects to asthma. Observations of Koenig et al. (1990) and Molfino et al. (1991) suggest the possibility that acute exposure to ozone at a dose

(0.12 ppm with or without exercise) that does not produce measurable pulmonary function decrements may increase the responsiveness of asthmatics to subsequently inhaled SO_2 or allergens. Contrary to these findings, Bascom et al. (1990) found no increase in responses to antigen nasal challenge in a group of allergic subjects pre-exposed to 0.5 ppm ozone for 4 h when compared to air-antigen challenge.

The overall animal data provides strong evidence that the ozone-induced enhancement in responsiveness is mediated, at least in part, by cholinergic receptors on airway smooth muscle. Osebold et al. (1980) hypothesized that the increased epithelial permeability caused by ozone may allow greater penetration of bronchoconstriction substances, resulting in increased airway responsiveness.

It has also been postulated that ozone-induced acute inflammation may be important in the induction of the increased airway responsiveness (U.S. EPA, 1996). Ozone (0.4 ppm)-induced rapid increase in prostaglandin (PGE_2), a mediator involved in bronchoconstriction, in BAL has been reported in a number of studies (McDonnell et al., 1991a,b; Hazucha et al., 1996; Devlin et al., 1996; Devlin et al., 1997), except for one study by Coffey et al. (1996) who did not observe any alteration in PGE_2. It also appears that increased bronchial reactivity is a consequence of cellular or biochemical changes in the airway, and does not correlated with spirometric responses (Aris et al., 1995; Jorres et al., 1996). Because these alterations are part of a complex process, it comes as no surprise that the mechanistic studies on ozone-induced increases in airway responsiveness have not pinpointed an isolated derangement.

11.4 INFLAMMATION AND HOST DEFENCE

Inflammation can be considered as the host response to injury, and the induction of inflammation can be accepted as evidence that injury has occurred. Inflammation induced by exposure of humans to ozone can have several outcomes:

- inflammation induced by a single exposure (or several exposures over the course of a summer) resolves entirely;
- continued acute inflammation evolves into a chronic inflammatory state;
- continued inflammation alters the structure or function of other pulmonary tissue, leading to diseases such as fibrosis or emphysema;
- inflammation alters the body's host defence response to inhaled microorganisms, particularly in potentially vulnerable populations such as the very young and old;
- inflammation alters the lung's response to other agents such as allergens or toxicants.

It is also postulated (U.S. EPA, 1996) that the profile of response can be altered in persons with pre existing pulmonary disease (e.g., asthma or COPD) or smokers.

The presence of polymorphonuclear leukocytes (PMN) in the lung has long been accepted as a hallmark of inflammation and has been taken as the major indicator that ozone causes inflammation in the lungs of humans. Soluble mediators of inflammation such as cytokines (Interleukin-6, -8, -1, and tumour necrosis factor) and arachidonic acid metabolites (e.g., PGE_2, $PGF_{2\cdot}$, throboxanes, leukotrienes) have also been measured in the BAL fluid of humans exposed to ozone. In addition to their role in inflammation, many of these compounds have bronchoconstrictive properties, and may be involved in increased bronchial hyperreactivity observed following ozone exposure.

Under normal circumstances, the epithelia lining the large and small airways develop tight junctions and restrict the penetration of exogenous particles and macromolecules from the airway lumen into the interstitium and blood, as well as restricting the flow of plasma components into the airway lumen. Several studies report that ozone disrupts the integrity of the epithelial cell barrier in human airways, as measured by increased passage of radio labelled compounds out of the airways, as well as passage of markers of plasma influx such as albumin, immunoglobulin, and total BAL fluid protein into the airways. Markers of epithelial cell damage such as LDH have also been measured in the BAL fluid of subjects exposed to ozone.

Inflammatory cells of the lung such as macrophages, monocytes, and PMN also constitute an important component of the pulmonary host defence system. Upon activation, these cells not only are capable of generating free radicals and enzymes with microbicidal activities, but also have the potential of damaging nearby cells. On the other hand, damage of these cells may inhibit microbicidal function, and enhance the susceptibility to bacterial infection.

Other soluble factors that have been studied include those involved with fibrin deposition and degradation (tissue factor, factor VII, and plasminogen activator), potential markers of fibrogenesis (fibronectin, platelet derived growth factor), and components of the complement cascade (C3a).

It should be noted that existing evidence has shown that airway inflammatory responses are not correlated with decrements in FEV_1 (Aris et al., 1993; Balmes et al., 1996; Hazucha et al., 1996). 'Responders' (substantial decrement in FEV_1 in response to ozone) may not necessarily have higher inflammatory responses than 'non responders' (little decrement in FEV_1 after ozone exposure). The mechanism of FEV_1 and FVC decrements are thought to involve neurally mediated involuntary inhibition of inspiration and reduction of vital capacity (Hazucha et al., 1989). Therefore, assessment of ozone-induced health effects using spirometric parameters may have measured a reflexive rather than adverse physical response. Since the US National Ambient Air Quality Standard (NAAQS) for ozone was established largely based on spirometric responses to ozone inhalation, some researchers have suggested rethinking the NAAQS setting process for ozone.

11.4.1 Inflammation Assessed by Bronchoalveolar Lavage

Two early studies (Seltzer et al., 1986; Koren et al., 1989a,b) demonstrate that exposure of humans to high levels of ozone (0.4 to 0.6 ppm, with exercise for 2 h at $\underline{V}_E$ 70 L/min; BAL were performed 3 and 18 hours post exposure respectively for each study) results in an inflammatory reaction in the lung, as evidenced by substantial increases in neutrophils and proinflammatory compounds.

Numerous studies published during the following years have provided further evidence to support these observations (Hatch et al., 1994; Fahy et al., 1995; Weinmann et al., 1995a; Hazucha et al., 1996; Devlin et al., 1996; Coffey et al., 1996; Devlin et al., 1997). Moreover, new studies also demonstrate that at moderate (0.2 - 0.25 ppm for 1 - 4-hours, at $\underline{V}_E$ 40 - 60 L/min) concentrations of ozone, both inflammatory cells and mediators capable of damaging pulmonary tissue integrity increased significantly in healthy young subjects after ozone exposure, as did compounds that play a role in fibrotic and fibrinolytic processes (Hazbun et al., 1993; Aris et al., 1993; Scannell et al., 1996; Balmes et al., 1996; Torres et al., 1996).

Asthmatic patients are revealed more sensitive toward ozone-induced airway inflammation than healthy subjects (Basha et al., 1994; Scannell et al., 1996). At concentrations of 0.12 to 0.24 ppm (90 minutes at $\underline{V}_E$ • 50 L/min, and 6-hours at $\underline{V}_E$ • 25 L/min) ozone induced higher inflammatory responses in asthmatics than in healthy subjects (Basha et al., 1994; Scannell et al., 1996).

Kehrl et al. (1987) demonstrate that human pulmonary epithelial cell permeability was increased as measured by increased clearance of ^{99m}Tc-DTPA (diethylene triamine pentaacetic acid), following the exposure to ozone (0.4 ppm for 2-hours with exercise $\underline{V}_E$ 70 L/min). Kehrl et al. (1989) reported similar observation on an additional 16 subjects. For the combined group of 24 subjects, exposed to 0.4 ppm for 2-hours (with heavy exercise, $\underline{V}_E$ 70 L/min), the average clearance rate was 60% faster than that observed after air exposure, strongly suggesting increased permeability from the airway lumen and alveolar space to the blood and interstitial spaces. The average ozone-induced decrement in FVC in these subjects was 10%.

Recently published data by Foster and Stetkiewicz (1996), despite using a different dose regimen, observed similar results. Foster and Stetkiewicz (1996) exposed healthy subjects (mean age 26 years, n = 9) to filtered air or ozone (initiated at 0.15 ppm, ramped to 0.35 ppm, then returned to 0.15 ppm) during a 130 minute intermittent exercise ($\underline{V}_E$ at 40 L/min). ^{99m}Tc-labelled DTPA solute was deposited by aerosol on the epithelial surfaces 18 to 20 hours later. The lung clearance of ^{99m}Tc-DTPA over a 120 minute period was significantly faster compared with air control. Regional analysis demonstrated that ^{99m}Tc-DTPA clearance from the periphery (excluding the lung hilum) and lung apexes were significantly increased by ozone but changes in clearance for the base of the lung were not significant. Their data support the observations by Kehrl et al. (1987, 1989) indicating that epithelial permeability of the lung is altered by ozone exposure. Moreover, this injury happens at relatively low ozone concentrations, and is regional in lungs. These changes in permeability are likely associated with acute inflammation and may potentially allow better access of inhaled antigens and other substances to the mucosa.

Macrophages exposed *in vivo* showed changes in 123 proteins (Koren et al., 1989a). Exposure to 0.22 ppm ozone for 4-hours has been reported to initiate the generation of superoxide anion by the total BAL cells (Torres et al., 1996). Exposure to 0.4 ppm ozone for 2-hours ($\underline{V}_E$ at • 60 L/min) increased production of lipoxygenase metabolites by alveolar macrophages (Coffey et al., 1996). These data are suggestive of mediator activation of the macrophage *in vivo*. However, in terms of alveolar macrophage function, other researchers have observed an ozone-induced reduction of macrophage function, indicated by a decrease in the ability of alveolar macrophages to phagocytes

Candida albicans after exposure to 0.4 ppm ozone for 2-hours ($\underline{V}_E$ at 66 L/min) (Devlin et al., 1996), and a reduction in production of hydrogen peroxide in alveolar macrophages after exposure to 0.22 ppm ozone for 4-hours (Torres et al., 1996). Therefore, exposure to ozone may impair the endogenous microcidal function.

Based on data obtained from experimental animal studies, airways have been shown to be a major site of ozone-induced inflammation. However, few human studies have confirmed this finding because BAL primarily samples cells and fluid in the terminal alveoli and bronchioles (U.S. EPA, 1996). Recently, studies investigating inflammatory responses in bronchus proximal airway lavage (PAL), bronchial fraction and BAL (Aris et al., 1993; Scannell et al., 1996; Balmes et al., 1996) demonstrate that there is a regional difference in inflammatory effects in response to ozone insult. While exposure of healthy and asthmatic subjects to ozone (0.2 to 0.25 ppm ozone for 1 to 4-hours) initiated the influx of PMN occurs in all the airway regions, the increased release of small inflammatory mediators and molecules such as interleukins, total proteins, LDH (a cell death indicator), and fibronectin was more likely to take place in BAL (Balmes et al., 1996; Scannell et al., 1996). Additionally, Aris et al. (1993) found that more total cells, neutrophils and epithelial cells appeared in PAL fluids than in BAL, and a significant increase of LDH in PAL after exposure to 0.2 ppm ozone (4-hours), suggesting an ozone-induced neutrophil influx coupled with ozone-induced epithelial cell shedding. Ozone injures proximal airways as well as the distal lung.

Numerous studies have shown the 'adaptation' or 'tolerance' phenomenon in pulmonary function decrements following daily consecutive exposure to ozone (see 11.1.5). Experimental animal studies (Tepper et al., 1989; VanBree et al., 1994) have suggested that although some markers of inflammation may be diminished after repeated ozone exposure, underlying damage to lung epithelial cells may continue. There are very limited data on human 'adaptation' to ozone-induced inflammation. In a recently published report (Devlin et al., 1997), healthy human subjects (n = 16) were exposed to 0.4 ppm ozone for 5 consecutive days (2-hours/day) while undergoing intermittent exercise ($\underline{V}_E$ at 60 L/min). Ten or 20 days later, subjects were exposed to ozone a single time. The results show that numerous indicators of inflammation were attenuated. After 5 days of exposure, ozone-induced increases in %PMN, IL-6, PGE_2, elastase, fibronectin were diminished, when compared with a single exposure to the same dosage of ozone (Devlin et al., 1996). Ozone-induced decreases in recovery of viable BAL cells and alveolar macrophage phagocytosis of yeast were also blunted by the repeated exposure. Within 10 to 20 days, %PMN, IL-6, PGE_2, fibronectin, and recovery of viable cells showed at least partial reversal, while other mediators did not return to the normal response to ozone. Thus, biochemical mediators in response to ozone were attenuated after 5 consecutive days of ozone exposure. The attenuation of inflammation is similar to attenuation of symptoms and lung function responses. In agreement with animal studies, some cell injury markers (LDH, elastase) did not show adaptation, indicating that tissue damage may continue to occur during repeated exposure.

11.4.2 Inflammation Induced by Ambient Levels of Ozone

Devlin et al. (1991) reported an inflammatory response in humans exposed to levels of ozone at 0.12 ppm or below. In this study, healthy subjects were exposed to 0.08 and 0.1 ppm ozone for 6.6-hours with moderate exercise ($\underline{V}_E$ 40 L/min), and underwent BAL 18 hours later. Increased numbers of PMN and levels of IL-6, fibronectin and PGE_2, and decreased alveolar macrophage phagocytic capability were found at both ozone concentrations. When data are normalized for concentration, exposure duration and $\underline{V}_E$, and compared with the data reported by Koren et al. (1989a,b) (0.4 ppm ozone exposure for 2-hours with intermittent exercise at $\underline{V}_E$ 70 L/min), the inflammatory changes observed in these studies suggest that lung inflammation from ozone may occur as a consequence of exposure to ambient levels while exercising.

There is a considerable variation of response among the individuals in the Devlin study, some showing little or no response to ozone and others having increases in IL-6 or PMN that were as large or larger than those reported by Koren et al. (1989a,b). Individuals with the largest increases in inflammatory mediators in this study did not necessarily have the largest decrements in pulmonary function, suggesting separate mechanisms underlying physiological and inflammatory responses to ozone.

These data further suggest that, although the population as a whole may have a small inflammatory response to low levels of ozone, there may be a significant subpopulation that is very sensitive to these low levels of ozone. Furthermore, even a small inflammatory response (if it recurs) in the population as a whole should not be discounted. Such a response in people with severely compromised respiratory systems may result in sustained adverse health effects. Although this has not yet been documented in chamber studies (only mild asthma cases have been used for the chamber studies), we cannot dismiss the potential of ozone to affect moderate and severe asthma through this process.

11.4.3 Time Course of Inflammatory Response

As summarized by the U.S. EPA (1996), some data show that the inflammatory response is quickly initiated 1 hour (Devlin et al., 1990; Koren et al., 1991) to 3 hours (Seltzer et al., 1986), after a 2-hour exposure to 0.4 ppm of ozone. Inflammatory mediators (IL-6) and cells (PMN) remain elevated 18 hours after exposure (Koren et al., 1989a,b). These studies also show that there is a difference in the magnitude of response of some indicators depending on when the BAL is performed after exposure to ozone. Increases of PMN, IL-6, and PGE_2 are greater after 1 hour, fibronectin and plasminogen activator are greater after 18 hours, and protein and Tissue Factor are equally elevated at both times. A study by Schelegle et al. (1991) suggests that the percent of PMN may be elevated early (1 to 6 hours post exposure to 0.3 ppm ozone for 1-hour with mouth piece) in proximal airways and later (6-24 hours post exposure) in distal airways and alveolar surfaces. These results are preliminary and include data from only 5 subjects.

In a recent study conducted by Coffey et al. (1996), the researchers investigated inflammatory changes in BAL at 0, 2 and 4 hours after a 2-hour exposure to 0.4 ppm ozone with intermittent exercise ($\underline{V}_E$ • 60 L/min). The volunteers were 11 healthy nonsmokers, age 18 - 35 years. There was a time-dependent increase in the number of PMN, and a significant reduction in the number of alveolar macrophages following ozone exposure, with the highest changes occurring at 4 hours after exposure. The levels of leukotrienes [LTC_4 (a substance of anaphylaxis) and LTB_4 (a potent chemotactic agent inflammatory cells)] were significantly higher at 0 hour following ozone exposure compared to air, with no change in prostaglandins. At 4 hours after the end of ozone exposure, LTB4 level returned to normal level.

Devlin et al. (1996) compared changes of inflammatory mediators in BAL 1 and 18 hours after a 2-hour exposure to 0.4 ppm ozone. Eight healthy subjects, at the age of 18 to 35 years, were studied during intermittent exercise ($\underline{V}_E$ 66 L/min). The data reveal that ozone induced rapid increase in PMN, protein, LDH, α-1 antitrypsin, fibronectin, PGE_2, thromboxane B_2, C3a, tissue factor and clotting factor VII one hour after exposure. There was a decrease in recovery of total cells and alveolar macrophages, and decreased ability of alveolar macrophages to phagocytes *Candida albicans*. Compared with data collected 18 hours after exposure, IL-6 and PGE_2 levels were higher 1 hour after exposure than 18 hours after exposure, while fibronectin and tissue-plasminogen activator levels were higher 18 hours after exposure, and the PMN, proteins, and C3a were present at essentially the same levels at both times. The researchers concluded that several inflammatory mediators are already elevated 1 hour after exposure, and some mediators achieve their maximal levels in BAL fluid at different times following exposure.

Torres et al. (1996) examined the time pattern of airway inflammation following exposure to a moderate level of ozone (0.22 ppm, 4-hours, with exercise). Healthy nonsmokers were classified as responders (>15% fall in FEV_1 following ozone exposure, n = 12) and non-responders (<5% fall in FEV_1 after ozone exposure, n = 12). Subjects were exposed to air and ozone in separate days. BAL was performed immediately and 18-hour after ozone exposure, and either early or late after air. The concentration of PMN in BAL increased nearly five fold 18 hours after ozone exposure in both responders and non-responders. In responders, stimulated superoxide anion production in lavage cells increased progressively, with the highest level at 18 hours after ozone exposure. Unstimulated hydrogen peroxide production in alveolar macrophage from responders decreased progressively, and in a time-dependent fashion. There were no significant changes in reactive oxygen intermediate production by cells from non-responders. Therefore, influx of PMN may increase the burden of reactive oxygen intermediate to the airway epithelium. The authors speculate that both the number of alveolar macrophages and the production of reactive oxygen intermediates in alveolar macrophages were down-regulated following exposure in ozone responders, thus limiting the potential for injury to the alveolar epithelium.

11.4.4 Effects of Anti-Inflammatory Agents on Ozone-Induced Inflammation

Hazucha et al. (1996) studied the effect of ibuprofen, a non-steroid anti-inflammatory agent, on ozone-induced inflammatory responses. Ten healthy subjects (20 to 32 years of age) were given 800 mg of ibuprofen or placebo and were exposed to filtered air and 0.4 ppm ozone for 2-hours with intermittent exercise ($\underline{V}_E$ at • 60 L/min). Data obtained from this study show that although anti-inflammatory agents may blunt ozone-induced decrements in FEV_1 and increases in PGE_2, most inflammatory and cell injury parameters (PMNs, fibronectin, permeability, LDH, or macrophage phagocytic function) were not affected by ibuprofen in the BAL of these subjects. Ozone-induced increases of airway resistance was not affected by ibuprofen treatment either.

In agreement with the above observation, data from Liu et al. (1997a) demonstrate that pre-treatment of healthy subjects with acetylsalicylic acid (ASA, 0.975 g) did not suppress 0.4 ppm ozone-induced increase in PMN and decrease in macrophages sputum, although the pre-treatment with ASA inhibited 0.12 ppm ozone-induced increase in airway resistance (Liu et al., 1997b).

The above evidence suggests that:

1. ozone initiates pulmonary function decrements and airway inflammation via different mechanisms;
2. spirometric changes may not reflect pulmonary tissue injury; and
3. pre-treatment with non-steroid anti-inflammatory agents, may blunt pulmonary function changes and relieve some symptoms, but may not represent a protective mechanism against ozone-induced lung injury.

11.4.5 Use of Nasal Lavage (NL) to Assess Ozone-Induced Inflammation in the Upper Respiratory Tract

Bronchoalveolar lavage, the most frequently used method for studying lower airway damage, is an invasive procedure, and may alter some endpoints due to local anaesthesia. Since nasal lavage procedure is non-invasive, it has been proposed to be a sensitive and reliable tool to detect inflammation in the upper airways of humans exposed to xenobiotics. In summary of the U.S. EPA document (1996), limited studies using nasal lavage method demonstrate elevated PMN following exposure to 0.4 to 0.5 ppm ozone. One study (Graham and Koren, 1990) demonstrated a good qualitative correlation between changes in PMN using both BAL and NL methods on the same subjects who were exposed to 0.4 ppm ozone for 2-hours (exercise $\underline{V}_E$ at 70 L/min).

Folinsbee et al. (1994) exposed 17 healthy non smoking male subjects to filtered air or 0.12 ppm ozone for 6.6-hours on 5 consecutive days with exercise ($\underline{V}_E$ 39 L/min). Nasal lavages were obtained before and after exposure, and did not reveal significant increase in PMN numbers after ozone exposure.

McBride et al. (1994) studied the inflammatory response in nasal lavage from 10 asthmatic (18 to 41 years old) and 8 non asthmatic (18 to 35 years old) subjects. Subjects were exposed to 0.12 and 0.24 ppm ozone or air for 90 minutes (exercise $\underline{V}_E$ 23 L/min). Nasal lavage was performed immediately and 24 hours after exposures. In asthmatic subjects, a significant increase in the number of white blood cells in lavage fluid was detected both immediately and 24 hours after exposure to 0.24 ppm ozone, as was a significant increase in epithelial cells immediately after exposure. No significant differences in levels of IL-8 were seen in the nasal lavage fluids after exposure to any of the three test atmospheres. A significant correlation was observed between IL-8 and white blood cell counts after exposure to 0.24 ppm ozone ($r = 0.76$). Histamine, LTB4 or platelet-activating factor were not detected in any of the nasal lavage samples. In non asthmatic subjects, no significant cellular changes were seen. No changes in pulmonary and nasal functions were detected in either group. These data are consistent with studies using BAL technique, indicating that asthmatic patients are more sensitive toward ozone-induced airway inflammation than healthy subjects (Basha et al., 1994; Scannell et al., 1996).

These studies suggest that nasal lavage may serve as a sensitive and reliable tool to detect inflammation in the upper airways of humans exposed to air pollutants, even at ozone concentrations which do not initiate spirometric responses.

11.4.6 Changes in Host Defence Capability Following Ozone Exposure

Concern about the effect of ozone on human host defence capability derives from numerous animal studies demonstrating that exposure to as little as 0.08 ppm ozone increases mortality in rodents subsequently challenged with aerosolized or instilled bacteria (Gardner et al., 1982; Van Loveren et al., 1988). In humans, Henderson et al. (1988) exposed 24 young males to inoculations of type 39 rhinovirus administered as nose drops. Half were then exposed to 0.3 ppm ozone (6-hours/day) for 5 consecutive days with intermittent light exercise and the other half were exposed to clean air under the same conditions. Nasal lavage was performed on the morning of days 1 to 5, 8, 15 and 30. No differences in virus titres, PMNs, or interferon gamma in nasal lavage fluid were noted between the groups. No difference in blood lymphocyte proliferative response to viral antigen were found in two groups. Other studies have shown that acute *in vivo* exposure of humans to ozone results in impairment of alveolar macrophage host defence capability, potentially resulting in decreased ability to phagocytose and kill inhaled microorganisms *in vivo*.

Although there are several studies in which animals have been exposed to bacteria or viruses in conjunction with ozone exposure, which provide some evidence to suggest that ozone impairs the immune system's ability to fight viral infections, there is insufficient human data to know whether ozone exposure affects viral infectivity. However, there is potential cause for concern that ozone may render humans and animals more susceptible to a subsequent bacterial challenge.

In terms of alveolar macrophage function, several researchers have observed an ozone-induced reduction of macrophage function. Torres et al. (1996) exposed healthy non smoking subjects (n = 24) to air and ozone (0.22 ppm for 4-hours with exercise). BAL was performed immediately and 18 hours after ozone exposure, and either early or late after air. Data show a progressive decrease in hydrogen peroxide production in alveolar macrophages in some subjects. Devlin et al. (1996) also found a significant decrease in the ability of alveolar macrophages to phagocytes *Candida albicans* after exposure to 0.4 ppm ozone for 2-hours (Devlin et al., 1996).

11.5 EXTRAPULMONARY SYSTEMIC EFFECTS OF OZONE

It is believed that ozone immediately reacts on contact with airway surface liquid and tissue, and is not absorbed or transported to extrapulmonary sites to any significant degree (Pryor 1992). Nevertheless, the demonstration in the previous section of an array of inflammatory modulators released at the airway surface provides a possible mechanism for effects to occur elsewhere in the body. Additional *in vivo* studies are needed, therefore, to determine if there are significant extrapulmonary effects of ozone exposure in humans and at what levels of exposure they may occur.

Liu et al. (1997b) studied the plasma concentrations of hydroxylated salicylate metabolites (an indicator for hydroxyl radical production *in vivo*) in healthy subjects exposed to 0.12 and 0.4 ppm ozone or air for 2-hours. They found that exposure to both 0.12 and 0.4 ppm ozone was associated with a significant increase in plasma 2,3-dihydroxybenzoic acid concentration, suggesting an increased production of hydroxyl radical in the body, although most likely occurring in lungs.

Foster et al. (1996) investigated several blood borne markers for ozone exposure. Healthy male subjects (mean age of 26 years, n = 10) were exposed to air or ozone over 3 consecutive days (130 min/day) with intermittent exercise (42 L/min for air, 44 L/min for ozone). Ozone level was varied at 20 minute intervals, from 0.25, 0.35, 0.45, 0.45, 0.35, to 0.25 ppm, and concluded with 10 minutes at 0.25 ppm. Blood was obtained before exposures on day one, immediately after exposure each day, and 18 to 20 hours after the third day of exposure. Markers measured include serum antioxidant α-tocopherol as a gauge of oxidative stress, and the blastogenic activity of peripheral blood monocytes as an index of immune function in response to ozone exposure. Twenty-hours after the third day of ozone exposure, α-tocopherol levels were reduced significantly compared with the air control subjects. Mitogen-activated T lymphocytes exhibited a 61% increase in blastogenic activity after 3 days of ozone exposure in comparison with the levels in air control or before ozone. The progressive increase in the expression of these systemic biomarkers may represent essential features of oxidant injury and/or repair.

Hazbun et al. (1993) exposed 7 healthy non smoking subjects (22 to 30 years old) to air and ozone (0.25 ppm for 1-hour) with heavy exercise ($\underline{V}_E$ • 60 L/min). They did not observe significant changes in plasma levels of substance P, 8-epi-$PGF_{2\alpha}$, C3a and C5a after ozone exposure, although in airway lavage fluid there were significant increases in concentrations of these mediators and protein.

Vender et al. (1994) examined the levels of glutathione and catalase in red blood cells following exposure of 7 healthy male subjects to 0.16 ppm or air for 7.5-hours. They did not find any significant changes in glutathione or catalase levels following ozone exposure. It appears that ozone-initiated health effects are most likely localized in the respiratory system.

11.6 SYMPTOMS AND PULMONARY FUNCTION IN CONTROLLED STUDIES OF AMBIENT AIR EXPOSURES

11.6.1 Mobile Laboratory Studies

The Rancho Los Amigos Medical Centre in California used a mobile laboratory for their field studies (U.S. EPA, 1996). These studies emphasize the importance of adequate characterization of subjects and the ambient air, exercise levels, duration of exposure, and individual variations in sensitivity when interpreting observed exposure effects. Although these factors need to be investigated over a wider range of experimental conditions, the results from these field studies are, so far, consistent with those from controlled human exposure studies. The effects include pulmonary function decrements at ozone concentrations of 0.144 ppm (1-hour) in healthy exercising ($\underline{V}_E$ 0.32 L/min) adolescents, and increased respiratory symptoms and pulmonary function decrements at 0.153 ppm (1-hour) in heavily exercising ($\underline{V}_E$ 53 L/min) athletes, and at 0.174 ppm (2-hours) in lightly exercising normal and asthmatic subjects. Many of the normal subjects with a history of allergy appeared to be more responsive to ozone than 'nonallergic' normal subjects, although a standardized evaluation of atopic status was not performed. These short term respiratory effects of summer ambient oxidant pollution in Southern California are believed to be predominantly, if not entirely, caused by ambient ozone in typical healthy or asthmatic residents according to mobile laboratory studies (Avol et al., 1984a, 1985). However, ambient air studies in the mobile laboratory are dependent on ambient conditions, which cannot be predicted, controlled, nor completely characterized.

11.7 SUMMARY AND CONCLUSIONS

Pulmonary responses observed during acute exposure to ozone at concentrations ranging from 0.10 to 0.50 ppm in healthy human subjects include decreases in TLC, IC, FVC, FEV_1, $FEF_{25-75\%}$, and V_T; and increases in SR_{aw}, breathing frequency, and airway responsiveness to methacholine challenge. Symptoms observed include cough, pain on deep inspiration, shortness of breath, throat irritation and wheezing. The physiological and symptom responses observed in the above studies can be separated in 5 different categories:

- symptoms,
- spirometric changes,
- airway resistance, and
- bronchial responsiveness to methacholine or antigen.
- airway inflammation

Inflammatory response detected in body fluids (BAL, nasal lavage, sputum) can also be observed directly. From the data collected, it appears that there is no correlation between spirometric changes and either airway resistance, bronchial responsiveness, or inflammation. Attenuation of airway resistance by atropine with no effects on spirometry (Beckett et al., 1985; Adams, 1986) coupled with the attenuation of spirometry response by indomethacin, Ibuprofen or ASA with no effect on airway resistance or responsiveness (Schelegle et al., 1987; Eschenbacher et al., 1989; Ying et al., 1990; Hazucha, 1996; Liu et al., 1997a and 1997b) support both this categorization and the notion of independent mechanisms.

The symptoms are often subjective measurements or simple reflex responses (cough), and are therefore difficult to correlate with objective physiological responses. However, cough and pain on deep inspiration have been related temporally to spirometry and breathing pattern responses.

11.7.1 Effects on Pulmonary Function

Healthy Subjects

Controlled human ozone exposure studies have provided strong and quantifiable exposure-response data on the health effects of ozone. The section on healthy subjects reviewed principally young adult subjects (18 to 35 years) exposed to ozone concentrations ranging from 0.08 to 0.75 ppm ozone either at rest or during continuous or intermittent exercise (20 to 90 L/min) protocols for durations of up to 8 hours. The major drawback of these studies is the small sample size. As a result, the conclusions derived from such studies may underestimate the actual response to low ozone concentrations in healthy young adults.

For resting exposures of a 2-hour duration, the effects noted include decreased FEV_1 and FVC at doses of 0.50 ppm or above.

For exercising exposures of a 1 to 4-hour duration, decreases in FEV_1 and FVC are observed at ozone concentration of 0.2 to 0.30 ppm for $\underline{V}_E$ of 30 to 50 L/min using intermittent exercise protocol (Aris et al., 1993; Hazbun et al., 1993; Fox et al., 1993; Aris et al., 1995; Balmes et al., 1996; Foster and Stetkiewicz 1996; Jorres et al., 1996; McKittrick and Adams, 1995; Frampton et al., 1997). At 0.12 ppm of ozone and $\underline{V}_E$ of ≥65 L/min using the same protocol, decrements in FVC, FEV_1 and pulmonary symptoms are observed (McDonnell et al., 1983). One study showed that exposure to 0.12 ppm ozone with a 2-hour intermittent exercise at $\underline{V}_E$ 45 L/min caused a significant increase in airway resistance (Liu et al., 1997b). Continuous heavy exercise ($\underline{V}_E$ = 55 to 90 L/min) for one hour has resulted in similar effects at 0.16 to 0.3 ppm ozone (McKittrick and Adams 1995).

Prolonged exposure (6 to 8-hours) has resulted in responses being observed at lower ozone concentration and lower ventilation rates. Responses are observed with ozone concentrations as low as 0.08 ppm using moderate intermittent exercise protocols ($\underline{V}_E$~ 35-40 L/min) (Folinsbee et al., 1988, 1991; Horstman et al., 1990; McDonnell et al., 1995). The symptoms and spirometry responses increase in a time, ozone concentration and $\underline{V}_E$ dependent pattern. Airway resistance is not always a sensitive parameter for exposure to ozone at concentrations up to 0.50 ppm with moderate or heavy exercise protocol.

Differences in responses between individuals, as well as the reproducibility of a response for each individual, have been documented. Healthy 'responders' have shown FEV_1 decrements at 0.12 ppm ozone during 2-hour intermittent exercise ($\underline{V}_E$ = 45 L/min), while 'non-responders' at this exposure regimen did not show any effects (Liu et al., 1997b). This suggests that some individuals are consistently more susceptible than others in their physiological response.

Group mean decrements in pulmonary function can be roughly estimated when expressed as a nonlinear (sigmoid) function of effective dose of ozone (ozone concentration x duration x $\underline{V}_E$) (McDonnell et al., 1993; McDonnell et al., 1995; Seal et al., 1996). The ozone concentration appears to have a greater impact on the pulmonary function response than does $\underline{V}_E$ or exposure duration. The exponent of approximately 4/3 suggests that doubling ozone concentration would be similar to increasing exposure duration by about 2.5 times (Larsen et al., 1991). Since at a given ozone concentration, the major external variables of spirometric response are $\underline{V}_E$ and exposure duration, and there is an intersubject variability in response, the models have not been able to estimate individual responses. Nevertheless, prediction of group mean FEV_1 responses using the variables of ozone concentration, duration and $\underline{V}_E$ can be successful. When taking into consideration duration and $\underline{V}_E$, a threshold ozone concentration below which no pulmonary function response would be elicited does not seem to exist.

Nevertheless, data from prolonged exposure (6 to 8-hours) at low ozone concentration (0.08 - 0.12 ppm) demonstrate that there is a plateau of FEV1 response to ozone for exposure duration. FEV1 response tends not to increase further with increasing duration of exposure, though the lung function decrements are in a ozone concentration-dependent linear fashion. The level of the response plateau is dependent upon ozone concentration and ventilation rate, and increasing ozone concentration can still enchance the response to beyond the existing plateau. Prolonged exposure studies at low dose suggest that ozone-induced spirometry responses depend upon the immediate exposure history.

Data from repeated exposure studies at higher concentrations (0.35 to 0.45 ppm) typically show that the spirometric response to ozone is enhanced on the second day of several consecutive days of exposure. At lower dose (0.12 ppm for 6.6-hours), this enhancement is observed on the first day and subsides on the second day, which may be explained by a more complete recovery and/or less damage to pulmonary tissues. The same studies have shown an attenuation of effects of ozone ('adaptation' or 'tolerance') after 3 to 5 days of exposure regardless of ozone dose rate, although attenuation occurs earlier at lower dose rates. Attenuation is partially reversed after 4 to 7 days post-exposure and normal responsiveness is returned within 1 to 2 weeks. The attenuation of bronchial responsiveness to methacholine challenge may occur somewhat more slowly than that of symptoms and spirometric responses.

In a study designed to compare the effects of varying and constant levels of ozone exposure (Hazucha et al., 1992), subjects were exposed to either air, a constant concentration of 0.12 ppm ozone, or a linearly variable concentration of ozone that ranged from 0 at start to 0.24 ppm at 4-hours and back down to 0 ppm at 8-hours (end of experiment). The workload of intermittent exercise was the same ($\underline{V}_E$ 40 L/min). At a constant 0.12 ppm of ozone, FEV$_1$ was decreased by 5% at the fifth hour until the end of the exposure period. In the variable concentration group, the FEV$_1$ decreased almost twice as much as the constant dose regimen, though the total concentration of ozone in two groups was the same. In essence, the results show that the average dose value calculated as a mean over an 8-hour exposure may underestimate the effect of ozone on FEV$_1$ and possibly other parameters (e.g., inflammatory response), when peaks are much higher than the averaged value over 8 hours. Although it is difficult to quantitatively determine spirometric responses to peak values in a epidemiological field study, the information obtained from the controlled human exposure studies is indicative of a potentially substantial health effect. The above data raise a concern about exercising people with increased $\underline{V}_E$. When taking into consideration the potential for exercising people to be exposed during a peak, it may increase their spirometric (e.g., FEV$_1$) and biological response (such as pulmonary injury). As such, they should be identified as a population sub-group more at risk.

The data from other authors (McDonnell et al., 1983) appear to show that a plateau is reached at a certain dose/time; FEV$_1$ decrements reach a plateau of 15-17% between 0.24 to 0.4 ppm exposure concentrations after 2.5-hour exposure. This may in fact mean that high peaks may not be able to produce effects larger than this. Since conditions of exposure are different in these studies, one must be careful when estimating the potential outcome of such peaks.

It has been hypothesized that there may be an overall sequence of events influencing the outcomes of ozone exposure on lung toxicity. Initially, ozone is delivered to the lung tissue where it then reacts with components in airway surface liquid and/or epithelial cell membranes. This then triggers local tissue responses including injury and inflammation. Finally, there is a stimulation of the neural afferent (bronchial C fibres) which results in a reflex response. The stimulation of C fibres, possibly through an increased sensitization of the cholinergic receptors, results in the contraction of the lung smooth muscle fibres which increases airway resistance. This is followed by rapid shallow breathing and increased frequency. These effects contribute to maintain a constant $\underline{V}_E$.

It is noteworthy that there exists evidence that airway inflammatory responses are not correlated with decrements in FEV_1 (Aris et al., 1993; Balmes et al., 1996; Hazucha et al., 1996). The inflammatory effects observed in 'responders' (substantial decrement in FEV_1) versus 'non-responders' (little decrement in FEV_1) are inconsistent. One study (Balmes et al., 1996) shows that there were similar increases in inflammatory cells and mediators in airway lavage fluids in responders and non-responders after exposure to 0.2 ppm ozone for 4-hours. Another study (Torres et al., 1996) indicates that responders had significantly increased superoxide anion production in lavage cells and reduced hydrogen peroxide production in alveolar macrophages after exposure to 0.22 ppm ozone (4-hours), whereas non-responders did not have significant changes in inflammatory cell function. Nevertheless, the number of PMN in BAL increased to a similar extent in responders and non-responders (Torres et al., 1996). Since ozone-induced FEV_1 and FVC decrements are thought to involve neurally mediated involuntary inhibition of inspiration and reduction of vital capacity (Hazucha et al., 1989), changes in spirometric parameters may not necessarily reflect cell injury. Since the US National Ambient Air Quality Standard (NAAQS) for ozone was established largely based on spirometric responses to ozone inhalation, some researchers have suggested rethinking the NAAQS-setting process for ozone.

Subjects with pre-existing disease

Of the subpopulations studied, those with pre-existing limitations in pulmonary function and exercise capacity are of primary concern in evaluating the health effects of ozone. Most of the studies available to date have definite limitations (e.g., subject selection, non-standardized method of characterization, limited dose-range) that preclude any final conclusion from being drawn.

For patients with COPD performing light to moderate intermittent exercise, early studies showed no decrements in pulmonary function after 1- and 2-hour exposures to ≤0.3 ppm ozone. A more recent study, however, shows that COPD patients had significantly greater loss of FEV_1 than their same age healthy counterparts (-19% versus -2%, respectively), when exposed to 0.24 ppm ozone for 4-hours during intermittent exercise ($\underline{V}_E$ = 20 L/min) (Gong et al., 1997b). COPD patients also showed moderate increase in symptoms and blood oxygenation which were not seen in healthy subjects (Gong et al., 1997b). This study suggests that COPD patients may be more sensitive to ozone exposure than healthy subjects.

For patients with asthma, data consistently show that no significant decrements in group pulmonary functions could be elicited with 40 minute to 2-hour ozone exposures ranging from 0.12 to 0.25 ppm, at rest or using light to moderate intermittent exercise ($\underline{V}_E$ 30 to 33 L/min) protocols, in both adults and adolescents. However, although the percent decrease in spirometry values was similar for healthy and asthmatic subjects after an acute exposure to an even higher effective dose of ozone (0.25 ppm for 3-hours, or 0.4 ppm for 2-hours), the asthmatic group had a pre-existing decrement of pulmonary function in comparison with healthy subjects (Kreit et al., 1989; Hiltermann et al., 1995; J• rres et al., 1996). Studies using a prolonged (6 to 8-hours, $\underline{V}_E$ approximately 30 L/min) exposure protocol have demonstrated that asthmatic subjects had more pronounced decrements in FEV1 than did healthy subjects in response to 0.12 to 0.16 ppm ozone (Linn et al., 1994; Horstman et al., 1995). Thus, if the total inhaled dose (or effective dose) is increased significantly by either increasing exposure duration or $\underline{V}_E$ during exposure, or ozone concentration, mild to moderate asthmatics will respond with a greater obstructive response than will normal subjects. Therefore, asthmatic subjects may be considered more susceptible and the average response of these subjects is probably more important, since their baseline values are already significantly depressed due to the underlying illness. Moreover, asthmatic subjects appear to have higher airway cellular responses (McBride et al., 1994) and higher responsiveness to allergens (J• rres et al., 1996) than healthy subjects, suggesting that exposure to ozone may facilitate the onset of asthma.

For patients with allergic rhinitis, data suggest that they have a greater rise in airway resistance than healthy subjects when exposed to 0.18 to 0.25 ppm ozone for 2 to 3-hours with intermittent exercise ($\underline{V}_E$ • 30 L/min). Allergen treatment substantiated ozone-induced FEV_1 decrement in these patients (J• rres et al., 1996).

11.7.2 Effects on exercise performance

A reduction of $\underline{V}O_{2max}$ has been observed after exposure to ozone (0.75 ppm for 2-hours) as well as a reduction in endurance. The ozone concentration that induces decrements in performance time during vigorous exercise can be as low as 0.06 ppm (duration 16 to 28 min) (Linder et al., 1988; Avol et al., 1984a). The actual mechanisms that lead to effects on exercise performance are not clear. Reports indicate that breathing discomfort associated with maximal ventilation may be an important factor in limiting exercise performance. This does not exclude the potential for a physiological mechanism to be responsible for these effects.

11.7.3 Effects on airway responsiveness

Ozone causes an increase in non-specific airway responsiveness which predisposes the airway to narrowing upon inhalation of a variety of stimuli. For young healthy subjects, increased airway responsiveness to histamine and methacholine has been observed following exposure to 0.20 ppm ozone for 1-hour (vigorous exercise) (Gong et al., 1986), and 0.08 to 0.12 ppm ozone for 6.6-hours with intermittent exercise ($\underline{V}_E$ 39 to 50 L/min) (Folinsbee et al., 1988; Horstman et al., 1990). In view of effective dose, elderly subjects appear to be less sensitive to ozone-induced airway responsiveness in comparison with young people.

Ozone exposure (0.12 ppm for 6.6-hours with exercise ~ $\underline{V}_E$ 29 L/min) of asthmatic subjects, who have increased baseline airway responsiveness, can cause further increases in responsiveness. The difference in baseline airway responsiveness between healthy and mild asthmatic subjects may be as much as 1000 fold, whereas the changes in airway responsiveness induced by ozone are typically 2 to 4 fold. Similar relative changes in airway responsiveness are seen in asthmatics exposed to ozone despite their markedly different baseline airway responsiveness. One of the important aspects of this observation of increase in airway responsiveness after ozone exposure is that this may represent a plausible link between ambient ozone exposure and increased hospital admissions for asthma.

The increases in airway responsiveness initiated by ozone exposure tend to resolve within 24 hours after exposure but may persist longer in some individuals. Changes in airway responsiveness after ozone exposure appear to be resolved more slowly than changes in FEV_1 or respiratory symptoms. In studies of repeated exposure to ozone, changes in airway responsiveness tend to be somewhat less susceptible to attenuation with consecutive exposures than changes in FEV_1. The question of whether chronic ozone exposure can induce a persistent increase (or decrease) in airway responsiveness has not been adequately studied.

Increases in airway responsiveness do not appear to be strongly associated with decrements in lung function or increases in symptoms. The mechanism of ozone-induced increases in airway responsiveness appears to be a consequence of cellular and biochemical changes in airway tissue.

11.7.4 Inflammation and host defence effects

Exposure to ozone (0.2 to 0.25 ppm for 1 to 4-hours, at $\underline{V}_E$ 40 to 60 L/min; 0.35 to 0.6 ppm, for 2 to 4-hours, at $\underline{V}_E$ 50 to 60 L/min) results in an inflammatory response characterized by increased numbers of PMNs, increased permeability of the epithelial cells lining the respiratory tract, cell damage, and production of proinflammatory cytokines and prostaglandins. This response can be detected as early as 1 hour after exposure and persists for at least 18 hours. The response profile of these mediators is not adequately defined, although it is clear that the time course of response varies for different mediators and cells.

Limited data have demonstrated that exposure to ambient levels of ozone (0.08 to 0.12 ppm) for 6.6-hours with exercise (40 - 45 L/min) can cause increases in inflammatory cells and mediators in upper and lower airways (Devlin et al., 1991). There is a considerable interindividual variation of inflammatory responses to ozone. These data suggest that although population as a whole may have a small inflammatory response to low levels of ozone, there may be significant subpopulation that is very sensitive to the low levels of ozone.

Asthmatic patients reveal more sensitive toward ozone-induced airway inflammation than healthy subjects. At concentrations of 0.12 to 0.24 ppm (90 minutes at $\underline{V}_E$ • 50 L/min, and 6-hours at $\underline{V}_E$ • 25 L/min), ozone induced higher inflammatory responses in asthmatics than in healthy subjects (Basha et al., 1994; Scannell et al., 1996).

The 'adaptation' phenomenon has been observed in inflammatory responses during repeated ozone exposure studies. Limited data show that after 5 consecutive days exposure to 0.4 ppm ozone, ozone-induced increase in cellular and biochemical parameters in BAL are attenuated, which can be partially reversed within 10 to 20 days. However, some cell injury markers did not show adaptation, implying a continuing tissue damage during repeated exposure, although spirometric parameters may return to a normal level.

In vitro studies suggest that epithelial cells are the primary target of ozone in the lung, and that ozone may induce them to produce many of the mediators found in human BAL fluid. Moreover, exposure to ozone at 0.2 to 0.4 ppm for 2 to 4-hours (with moderate to heavy exercise at $\underline{V}_E$ up to 66 L/min) has been found to cause the impairment of macrophage phagocytosis and hydrogen peroxide production, and hence may impair the endogenous antibiotic system.

11.7.5 Factors modifying responsiveness to ozone

None of the potential influences on ozone responsiveness (age, gender, race, hormonal fluctuations, smoking, seasonal variations in responsiveness, and ambient environmental factors) have been thoroughly investigated. However, the observation that healthy elderly adults appear to be less responsive to ozone exposure than young adults in spirometric parameters should be taken into consideration in risk assessment. No data have yet been reported on ozone-induced airway inflammatory changes in elderly subjects. In addition, responses of children and adolescents to ozone remain inadequately studied.

11.7.6 Extrapulmonary systemic effects of ozone

It is still believed that ozone immediately reacts on contact with respiratory system tissue and is not absorbed or transported to extrapulmonary sites to any significant degree.

11.7.7 Effects of ozone mixed with other pollutants

For simultaneous exposure to mixtures of ozone (0.12 to 0.6 ppm) with SO_2, NO_2, H_2SO_4, HNO_3, or particulate aerosols for 1 or 2-hours ($\underline{V}_E$ 25 - 40 L/min), or with multiple combinations of these pollutants, no significant enhancement of respiratory effects have been consistently demonstrated for these chemicals, i.e. response is not more than additive. Exposure to PAN at high levels (0.30 ppm) combined with ozone exposure has resulted in greater pulmonary function responses than ozone alone (Horvath et al., 1986). At ambient concentration, the effect of PAN appears negligible (Dreschler-Parks et al., 1989).

However, a study of exposure to ozone followed by SO_2 exposure has revealed an interaction between the two pollutants (Koenig et al.1990). The study shows that pre-exposure to ozone (0.12 ppm for 45 min, $\underline{V}_E$ 30 L/min) followed by exposure to a low concentration of SO_2 (0.1 ppm for 15 min) elicited a greater degree of bronchial hyperreactivity than did pure air followed by SO_2 or by two exposures to ozone alone; indicating some synergism between the effects of SO_2 and ozone. These results also can be interpreted, in view of the fact that ozone enhances non-specific bronchial responsiveness, to mean that the elevated SO_2 responses may simply reflect this increased responsiveness. Two studies investigating the effect of exposure to co-pollutants in a sequential pattern also show an additive effect of NO_2 (0.6 ppm for 2-hours) (Hazucha et al., 1994) and sulphuric acid (100 $\mu g/m^3$, for 3-hours) (Utell et al., 1994) on ozone (0.18 to 0.3 ppm, 45 minutes to 3-hours) induced spirometric responses. The exercise levels were at $\underline{V}_E$ 30 - 40 L/min.

The assessment of such mixtures is far from complete and much work remains to be done. Few studies have included more than two chemicals, and the endpoints measured are often limited to pulmonary function variables.

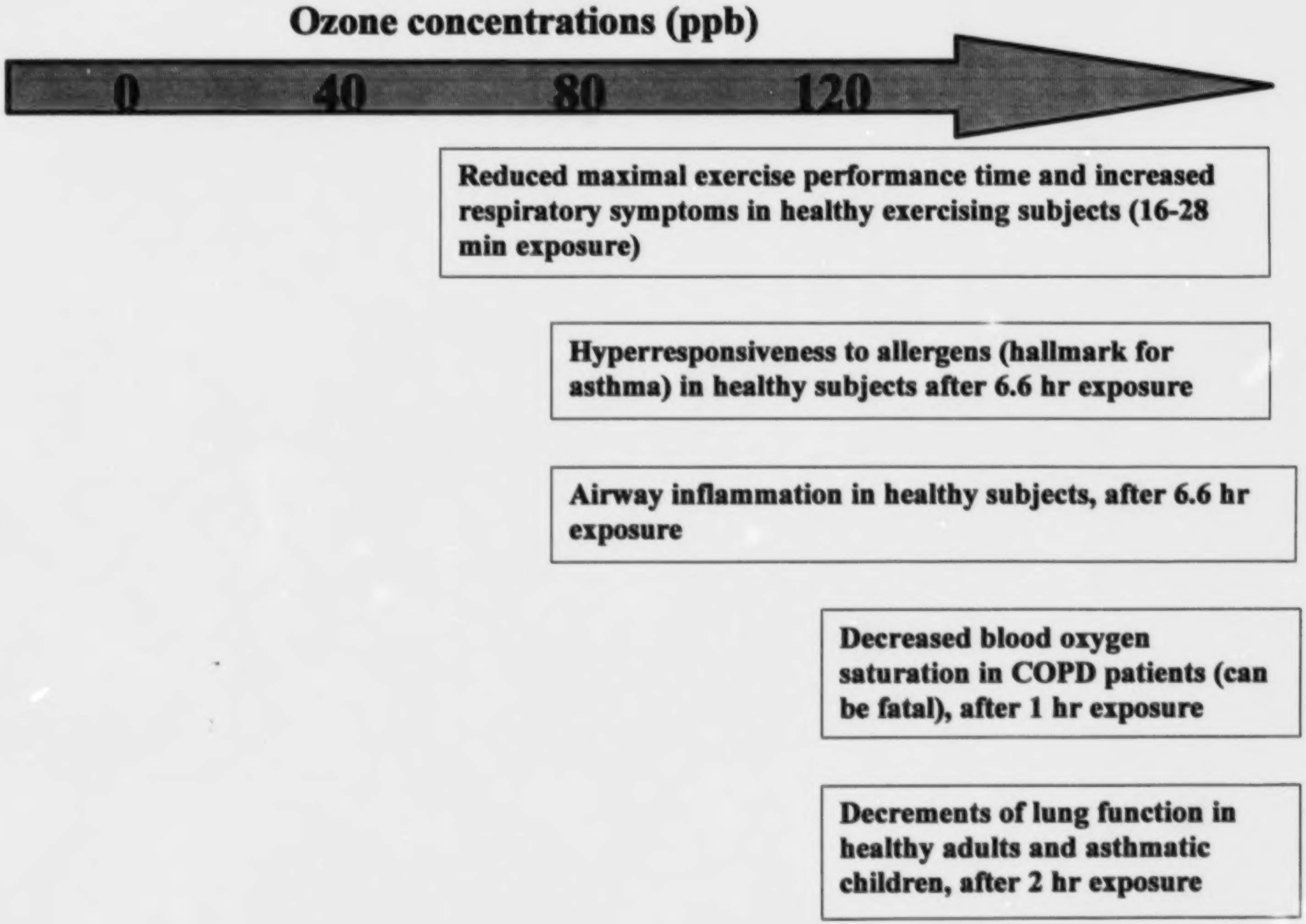
11.7.8 Conclusions

Overall, the responses observed in humans exposed to ozone can be separated into five different categories:

1. symptoms: cough, pain on deep inspiration, shortness of breath, throat irritation, and wheezing;
2. spirometric (spirographic) changes: decrements in FEV_1, FVC, and peak expiratory flow rate (PEFR);
3. airway resistance: increases in airway resistance (R_{aw});
4. bronchial responsiveness: to methacholine, allergens, sulphur dioxide, cold air, etc.; and
5. airway inflammation: changes in numbers and functions of inflammatory cells, and changes in mediator levels, measured in BAL and nasal lavage fluids and sputum.

The lowest doses reported in clinical studies that have induced health effects are summarized in Figure 11.3. It must be noted that no study on tissue injury, such as pulmonary inflammation, has been carried out at ozone concentrations below 80 ppb for healthy subjects, or below 120 ppb for asthmatics. These drawbacks limit the use of clinical data for predicting the health effects from ambient ozone exposure in a general population, or for establishing a lowest observed effect level (LOAEL) for ozone.

Figure 11.3 Summary of lowest doses of ozone reported to have induced health effects in human clinical studies.



Reduced maximal exercise performance time and increased respiratory symptoms in healthy exercising subjects (16-28 min exposure)

Hyperresponsiveness to allergens (hallmark for asthma) in healthy subjects after 6.6 hr exposure

Airway inflammation in healthy subjects, after 6.6 hr exposure

Decreased blood oxygen saturation in COPD patients (can be fatal), after 1 hr exposure

Decrements of lung function in healthy adults and asthmatic children, after 2 hr exposure

An important finding of the human clinical studies is that at a given ozone concentration, the increase in ventilation results in elevated pulmonary function responses and inflammation, and that increased ventilation lowers the concentration of ozone required for a given pulmonary response. Thus the concept of 'effective dose' is introduced, namely, a product of the ventilation rate, the concentration of ozone and the exposure duration ($\underline{V}_E$ x ozone concentration x duration). This concept allows us the opportunity to further establish models and to investigate the sensitivity of different ages, genders, and disease status in response to ozone exposure. This also implies that persons doing outdoor exercise during an ozone episode may be at higher risk due to their higher intake of ozone. This assumption has been confirmed by observations that exposure to ozone as low as 60 ppb for only 16 to 28 min caused a significant decrease in endurance to heavy exercise and a significant increase in symptoms.

Dose-response curves have been derived from several studies using different models (logistic model, exponential model, quadratic model, and the log regression model), all for spirometric responses. An analysis of all these models was performed by Highfill and Costa (1995) which shows the limitations of each model. In general, the models that include variables for concentration (C) and duration (T) of exposure show a better fit to measured values. Attempts by these authors to include the ventilation rate ($\underline{V}_E$) in the models are stated to have improved the models. The log regression model proposed by Larsen et al. (1991) appears to predict quite well the FEV_1 decrements under very specific conditions. More importantly, on the grounds of the 'effective dose', there does not appear to be a threshold for ozone-induced spirometric responses; a prolonged ozone exposure at a concentration ≤ 0.08 ppm (the current Canadian National Ambient Air Quality Objective for ozone) may still exhibit an adverse health effect.

In respect to the sensitivity of biological markers (parameters) for ozone-induced adverse health effects, data have demonstrated that prolonged exposure (6 to 8-hours) of healthy subjects to ambient levels of ozone (0.08 to 0.12 ppm) with intermittent exercise at $\underline{V}_E$ of 35 to 50 L/min may cause increased bronchial responsiveness to methacholine, increased inflammation in airway (BAL), and decreased FEV_1. For shorter exposure duration (1 to 4-hours) to ≤ 0.12 ppm ozone, a significant increase in bronchial responsiveness has been observed, while little or no response in pulmonary function is seen, and no data have been reported on inflammatory response. The symptoms are often subjective measurements or simple reflex responses (cough), and are therefore difficult to correlate with injury. Airway resistance is not always sensitive in response to up to 0.5 ppm ozone exposure. Compared with measurements of bronchial responsiveness and inflammation parameters in BAL, FEV_1 appears to be a most convenient, non-invasive, and relatively sensitive marker for ozone-induced response. There are several observations which support this assumption, and may assist us in determining the best approach to regulating ozone in Canada. The exposure levels of ozone associated with increases in the hospitalization rates due to asthma are in the same range as those associated with the FEV_1 decrements observed in chamber studies. A dose-response curve can be applied to FEV_1 decrements. Asthmatic subjects who have higher inflammatory responses and bronchial reactivity also have higher decrements in FEV_1 in comparison with healthy subjects.

However, numerous studies have shown that changes of FEV_1 do not correlate with cell injury endpoints and bronchial hyperresponsiveness in response to ozone exposure. 'Responders' to ozone-induced decrements in FEV_1 do not necessarily have higher level of pulmonary tissue injury in comparison with 'non-responders'. This hinders the evaluation of the toxicity of ozone using spirometric parameters (i.e., at which point does a decrement in FEV_1 reflect injury). Therefore, when assessing the risks associated with ozone exposure, it is preferable to consider incorporating all the data on inflammation, bronchial hyperresponsiveness and spirometric responses.

In terms of sensitive subpopulations, only asthmatic subjects have constantly revealed higher alterations in spirometric and inflammatory parameters, and bronchial reactivity than their healthy counterparts. Since asthmatic patients have lower baseline values for most of the spirometric parameters than healthy subjects, a further decrease in FEV_1 induced by ozone may carry the value below the threshold which is associated with asthma attacks. In light of the epidemiological data indicating an increase in hospitalization due to asthma during high ozone days in Canada (Burnett et al., 1994; Thurston et al., 1994a,b), we may conclude that asthmatic subjects are a sensitive subgroup for ozone exposure. Data for COPD patients and subjects with allergic rhinitis are scarce and often inconsistent, and hence preclude any final conclusions.

A limited number of clinical studies have investigated the age difference in response to ozone. It appears that adolescents are more sensitive to ozone-induced pulmonary function decrements when compared with adults using the same dose regimen. However, older adults (60 years or older) have not been demonstrated to be particularly more susceptible to ozone in pulmonary function changes than their younger counterparts when given the same dose, although no study has been done on age differences in inflammatory responses. At present, based on limited studies, age does not appear to be a major determinant of response to ozone exposure, however, more research needed to elucidate this aspects of the issue.

Studies using varying doses (0 to 0.24 ppm, back to 0 ppm) over an 8-hour exposure have demonstrated that FEV_1 decrements are almost twice as much compared with a constant dose of 0.12 ppm for the same duration. Hence, using average dose value may underestimate the effects of ozone on FEV_1, and likely on other parameters, such as inflammation. The above data raise a concern about exercising people with increased $\underline{V}_E$. When taking into consideration the potential for exercising people to be exposed during a peak, it may increase their spirometric (e.g., FEV_1) and biological response (such as pulmonary injury). As such, they should be identified as a population sub-group more at risk.

11.8 RESEARCH NEEDS

- Data on ambient-levels of ozone-induced pulmonary injury are very limited, and need to be expanded, to corroborate the findings in epidemiological studies. A majority of the BAL analyses so far have been carried out at ozone concentrations of 0.4 ppm or higher.

- More systemic studies, such as ones investigating cardiovascular effects, should be carried out to elucidate the mechanisms of ozone-induced cardiovascular mortality observed in epidemiological studies.

- More sensitive biological markers of tissue injury should be developed to link ambient levels of ozone exposure to adverse health effects, in order to enhance the sensitivity of human clinical studies.

- Much work needs to be carried out to assess the effects of air pollutant mixtures. So far, few studies have included more than two chemicals, and the endpoints measured are often limited to pulmonary function variables.

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NATIONAL AMBIENT AIR QUALITY OBJECTIVES FOR GROUND-LEVEL OZONE

SCIENCE ASSESSMENT DOCUMENT

A Report by
the Federal-Provincial Working Group
on Air Quality Objectives
and Guidelines

July, 1999

This document has been divided into a series of files for easier downloading from our web site.

Part 6 of 7

12 HUMAN HEALTH EFFECTS—EPIDEMIOLOGY STUDIES

There has been, in the past several years, an increase in scientific study of the epidemiology of air pollution, especially as it relates to mortality and morbidity as expressed by hospitalizations and emergency department visits. Although the primary concern of many of the papers was the adverse health effects of ambient particulate pollution, a large number also investigated the effects of ozone, which often co-occurs with particles as a part of the air pollution mixture. The U.S. EPA Criteria Review (U.S. EPA, 1996a) and the accompanying Staff Paper of the Office of Air Quality Planning and Standards (OAQPS) (U.S. EPA, 1996b) give an excellent review of papers published to 1993. They also include a summary review of older papers included in their previous Criteria Review of 1986 (U.S. EPA, 1986). However, a number of relevant papers were published between 1994 and 1997, including several on Canadian populations. For this reason, an independent assessment was undertaken for this document, emphasizing studies on mortality, hospitalizations, and emergency department visits from 1990 to 1997.[1]

12.1 DESIGN ELEMENTS

12.1.1 Time-series Studies vs. Cross-sectional Studies

Most of the recent epidemiological studies considering acute and short-term effects of air pollution on human health have been time-series studies in which the timing of an adverse health event (for example, hospitalizations) is studied in relation to short-term time trends in air pollution within a defined geographic area. Cross-sectional studies, in which rates of chronic disease or mortality are compared across geographic locations, have often been applied to examination of long-term or chronic effects and their relationship to air pollutants. Both types of studies are denoted as 'ecological', since they are both observational; that is, no control of the experimental conditions is possible, and both consider very large groups of people (thousands or millions) rather than individuals. No individual exposure analysis is usually available or possible due to the impracticality of obtaining information on so many people, and exposure is inferred from centrally located outdoor ambient monitoring stations.

A time-series analysis is by definition longitudinal in nature. Changes over time in an adverse health endpoint in a single population are followed as changes occur in concentrations of a pollutant over time (usually a very short time as in the studies included in this review, but long-term changes could also be followed by this method). The hypothesis being tested in the time-series study is that differences in time related to the pollutant levels are also associated with the outcome. In the cross-sectional study, differences between two or more populations in different locations exposed to different pollutant mixes are examined for changes in health outcome. The time-series analysis is less likely than the cross-sectional analysis to give biased results since the study population is the same over time, and acts as its own "control". However, other environmental factors and other causes of illness can confound the results and must be taken into account in the time-series as well as the cross-sectional analysis. There are relatively few confounders of exposure from one day to the next in a single population for time-series studies. There are many more opportunities for confounding in cross-sectional analyses. For instance, in cross-sectional analyses, local emissions can affect neighbourhoods differently. In addition, for cross-sectional analyses, other differences between two or more populations are harder to discern and control (e.g., differences in socioeconomic status, 'natural' illness rates unrelated to the substance being investigated, and in lifestyles between communities). The time-series analysis is therefore considered, despite its ecological nature, to be potentially a relatively stronger indicator of effects on public health than the cross-sectional study.

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[1] Some 1998 and 1999 references are noted in the text. These were incorporated in the review as "1997 in press" peer reviewed papers, and have been published since. Hence, the 1998 / 1999 dates.

The major weakness of ecological studies with respect to judgments regarding causality is the lack of a direct link between personal exposure to the toxic agent and the resulting health outcome on the individual. Ecological studies such as the time-series studies tell us the risk that a particular endpoint (e.g., hospitalizations) will be increased for the entire population if the average exposure for the entire population is increased by a certain amount. They do not tell us anything about individual exposure or individual risk. Inferences about causality are suggested, strengthened or weakened, but not directly proven (see Section 12.7.6. for discussions of causality). In compensation for this lack, the strength of the time-series study is its ability to examine the overall population responses of very large numbers of individuals to the agent under investigation and, thereby, gain an understanding of the public health impacts and risks to the population as a whole. Causality must be judged by making use of the sum of all the information available from all epidemiological, clinical, and toxicological studies to weigh the evidence.

12.1.2 Statistical Issues, Confound Factors and Co-variates

Observational studies try to find relationships between population or community health responses and some characteristic of the environment, in this case air pollution from ozone. The relationship is often expressed as relative risk. This estimate of risk describes an increase in, for example, non-accidental mortality of 0.9% **above** baseline non-accidental mortality rates. Therefore, it is often referred to as a **relative risk** estimate and the value reported as 1.009 (for a 10 ppb increase in ozone), where a value of 1.000 represents the baseline risk rate. An alternative expression of this estimate of mortality risk for ozone is .09% increase in risk per 1 ppb increase in ozone; this simple conversion is possible because, as stated above, the concentration-response relationship is linear. 95% confidence levels are used to measure the statistical significance and uncertainty of the RR. Since the observed relationships are often weak from a statistical point of view, and are vulnerable to confounding from factors such as seasonal cyclic variations and co-pollutants, a rigorous statistical analysis is necessary in order to detect an effect.

Daily mortality and morbidity (hospitalizations, emergency department visits, etc.) are usually highly cyclic, and undergo strong seasonal fluctuations, with events such as hospitalizations highest on very cold and very hot days. Ambient ozone concentrations also are highly seasonal, with their highest levels in summer, and lowest levels in winter. Such seasonal trends could bias the results, and they require some means of adjustment in order to study the question of whether there is any association or effect of ozone on these health endpoints. Otherwise the 'signal' would be indistinguishable from the background 'noise'.

A common method of removing cyclic variations in the data is prefiltering through the use of a multiday (e.g., 15-day or weighted 19-day) moving average, by subtracting this average from each data point prior to analysis. This is called a 'high pass' filter because it allows high frequency fluctuations (daily or weekly) to remain while removing the longer cycles from the data. Regressions with sine and cosine functions of various periodicities are also effective in removing seasonal variations in data. Seasonal dummy variables have been used, but they do not always control for within-season variability. Restriction of the analysis to one season or to a part of a season (one or two months) is another method to overcome seasonal variability (Kinney et al. 1995). A fourth method is the use of a nonparametric smoothing technique, using the LOESS (locally optimal estimating and smoothing scatter plots) method for estimation. This method is termed the STL method (Seasonal and Trend decomposition using LOESS) (Schwartz, 1995; Cakmak et al. 1998). By analyzing Toronto data on hospital admissions for 11 years using various techniques, Cakmak et al. (1998) showed that the ozone-hospitalization relationship was highly sensitive to the presence or absence of temporal adjustments for seasonal and day-of-week effects. The method of adjustment was not a critical factor; the STL/LOESS method gave the best fit to the data, followed by the high pass filter.

For ozone, the control of weather variables (temperature, humidity) has also proven to be very important. Ambient ozone is often highly correlated with temperature, and correlation coefficients can be greater than 0.6. Temperature can therefore be a prime confounding factor. Because of its high correlation with ozone, the separation of the two effects is often difficult to establish. If temperature is removed too early in the analysis before examining the relationship of ozone to the outcome, some part of the ozone effect is removed with it, and the relationship of ozone with the endpoint will be severely reduced or eliminated altogether (U.S. EPA, 1993; Lipfert, 1994). Inclusion of temperature in the regression analysis (rather than filtering it out beforehand) avoids this problem. On the other hand, because temperature is often independently associated with adverse health outcomes in a U-shaped dose response, with both very low and very high temperatures resulting in adverse health effects, some researchers have tried to adjust the effects of temperature by using non-linear models. This methodology has proven to be effective in teasing out the confounding effect of temperature (Moolgavkar et al., 1995; Anderson et al., 1996, Touloumi et al., 1997). Other variables include lag time, the duration between the exposure and the effect, should be included in the analysis, and most authors have investigated this aspect. Autocorrelation (pollution on one day is not independent of pollution the next day) is also likely to occur, and statistical methods are available to overcome this.

The detrended data are then examined using correlation analysis, regression analyses, or a combination of the two. Regression analysis has commonly been used in recent papers, preceded by correlation analysis in order to give some direction to the regression analysis. It is not obvious at this time which regression model best fits the data, and no one model has been selected as preferential. As stated by Thurston & Kinney (1995), "in time-series analysis no model is perfect, but some models are more wrong than others". Poisson regression has been extensively used in the mortality data because mortality is a rare event, following a Poisson distribution. Log normal distributions, and Ordinary Least Squares (OLS) regressions are also common for hospitalization data. The results do not appear to be very sensitive to which of these is used (Kinney et al., 1995; Lipfert, 1994).

Many of the most recent papers using administrative databases have made use of these more sophisticated statistical techniques, to good effect. Those studies that have not, must be weighed more lightly in view of the strong possibility that the findings are spurious, due to confounding.

Additionally, airborne pollution always occurs as a mixture of agents, of which ozone is only one. Particulate matter (PM) has been the co-occurring pollutant of greatest concern with respect to confounding of the relationship between ozone and adverse health endpoints. PM is independently associated with adverse health outcomes including mortality, hospitalizations and Emergency Department visits, from cardiovascular as well as respiratory causes. PM is sometimes also correlated with ozone concentrations. The degree of correlation between the various metrics of PM and ozone is somewhat dependent on the location, (i.e. importance of local sources versus long-distance transport via movement of entire air masses, seasonal effects, etc.). Additional difficulties in the inclusion of PM in analyses are presented by the variety of metrics that have been used to measure it, and some controversy over which size of particles is responsible for the observations of adverse health effects. Total suspended particles (TSP) was used most frequently in the past, but has been replaced in some U.S. locations and complemented in some Canadian locations by PM_{10}, $PM_{2.5}$ or sulphates. Coefficient of Haze (COH) was also formerly measured. Visibility has also been used as a predictor for fine particles ($PM_{2.5}$). The sulphate fraction of particles is valuable as a surrogate for fine particles. Particle strong acidity has been suggested as the species that is partly responsible for the effect of particles on health, but direct measurements are available in very few localities. In addition, the presence of ammonia, which can change the acidity, is almost never measured. Further major difficulties are presented by the 6-day monitoring schedule for PM followed almost universally throughout North America, which has made it difficult or impossible to include PM in regression analyses for daily changes in pollutants compared to daily changes in adverse health outcomes. Similarly, other co-occurring pollutants often, but not always, have long-term fluctuations in levels. Many authors have not investigated the modifying effects of one or more of NO_2, SO_2, or CO on outcomes associated with ozone, although measurements were often available.

12.1.3 Selection Criteria For Quantitative Analysis (Meta-Analysis)

Many studies have attempted to determine the influence of ozone pollution on human health, which involves estimation of a parameter [such as relative risk (RR)] in a concentration-response function, along with a measure of the uncertainty of the estimate [such as 95% confidence interval (95% CI)]. Because uncertainty decreases as sample size increases, combining data sets is expected to yield more reliable estimates of relative risk. Combining data from several comparable studies in order to analyze them together is often referred to as meta-analysis. A meta-analysis of the published studies is presented in this document for each category of health outcomes, based on the availability of the data, in order to evaluate whether they collectively indicate statistically significant associations for that outcome.

A list of criteria is used in this document to select studies for inclusion in the quantitative analysis, and, within selected studies, to select from among several reported results. A study is included in the quantitative analysis only if it:

1. measures daily mortality or hospitalization (i.e., is a time series study);

2. reports quantitative results for ozone;

3. is an original study (rather than a review paper or an abstract) in a peer-reviewed publication;

4. considers the entire population (rather than only a subset of the population) in the study location;

5. adjusts effects of some measure of seasonal cycle, temperature and relative humidity;

6. reports results from a co-pollutant model, including PM or some proxy for PM in the model with ozone; PM_{10} or $PM_{2.5}$ is preferable to other measures of particulate matter, and more pollutants in the model is preferable to fewer pollutants;

7. considers summer results when there are results from a whole year and from several seasons in the same study.

Reporting a statistically significant positive result for ozone is not a criterion for study selection, nor does statistical significance or size of relative risk affect the criteria for result selection within a study.

For meta-analysis, it is reasonable that a pooled estimate that combines the estimates from all selected studies, should give more weight to estimates from studies with smaller variances than those with larger variances. Variances provide an indication of the uncertainty associated with an estimated parameter. It also takes into account both the consistency of data and the sample size used to obtain the estimate, two key factors that influence the reliability of results.

12.2 MORTALITY STUDIES—ACUTE EFFECTS

Past acute episodes of air pollution, as in the London fog episodes of the early 1950s, have been linked to increased mortality due to the presence of particulate matter accompanied by sulphur dioxide. But until very recently, there have been only a few suggestive reports of associations between mortality and ozone pollution. Twenty-three studies reported as of April, 1997, were reviewed in detail (see Table 12.1a). The primary purpose of most of the studies was to examine the possible association of mortality with particulate matter, and relationships with ozone (or other co-pollutants) were reported as secondary findings. A summary of the results is presented in Table 12.1b for a more straightforward demonstration of the results.

Table 12.1b also lists the final selection of studies on mortality and the rationale for exclusion of some studies. During the analysis, reported RRs were converted as necessary so that all RRs were expressed in terms of a 1-hour maximum averaging period, so that they are directly comparable. The conversion was based upon the ratio of the mean concentrations experienced for each averaging time in that study area. If this concentration information was not available from a specific study, a conversion of 2.5 was used to convert 24-hour average RRs, and a conversion of 1.33 was used to convert 8-hour average RRs, based on past experience (Schwartz, 1997).

Sections 12.2.1 and 12.2.2 in this chapter discuss the merits and weaknesses of specific studies, and Section 12.2.3 discusses the effects of co-pollutants. Section 12.2.4 reports the results of meta-analysis of mortality studies.

Table 12.1a Ambient ozone and association with mortality

REFERENCE LOCATION TIME OF STUDY	OZONE, PPB	OTHER VARIABLES	STUDY DESIGN	RESULTS COMMENTS
Schwartz 1991 Detroit, Mich. (pop. 2,340,000) 10 years, 1973-82	Means of 1-h max. and daily mean (values not given) 2-3 monitors	TSP: 87 ug/m^3 (24-h mean) (daily TSP est. based on 6-day monitoring) SO_2: 12 ppb weather var. (temp, visibility, dew point) mean daily deaths 53/d	-daily deaths, excl. non-residents, accidents -Poisson regression analysis -author stated that included in regression (no details given) were terms for time trends in mortality, year, seasonal variation in weather, over dispersion, serial correlation, dummy variables for hot and cold days. -ozone, TSP and SO_2 regressed with a 1-day lag	"ozone was highly insignificant as a predictor of daily mortality" -Reanal. excl. winter months (not defined) did not improve correlation of ozone -TSP lagged 1 day was highly associated with daily mortality ($p<.0001$), and was independent of SO_2 Association of mortality with O_3 may have been attenuated because of method of accounting for seasonality in measurement and outcome variable. -TSP and SO_2 were both moderately high. O_3 was probably also moderately high, in the range 60-70 ppb for 1-h daily max., but TSP most important as predictor of mortality -No CO or NOx included in monitoring or analysis
Kinney & Ozkaynak 1991 Los Angeles Co. (pop. 7,477,000) 10 years, 1970-79	75 ± 45 (mean daily 1-h max.) (O_x –total oxidants) 8 monitors, whole county	KM (measure of particulates) 25±11 SO_2 15 ppb NO_2 69 ppb CO 8 ppm Weather var. (temp, rel. humidity, extinction coeff.) total deaths 152 ± 18/d respiratory 8 ± 4/d cardio-vasc. 87 ± 13/d	-total daily deaths excl. suicides, accidents daily deaths from cardiovasc., respiratory causes -multiple regression analysis -weighted 19-d filter (high-pass) for removal of seasonal trends in deaths and pollution vars. -day-of-week dummy variables, -autoregression terms, -carried out sensitivity analyses, different filtering, supplemental regressions	-oxidants (O_x) lagged 1 d were associated with total and cardio-vascular mortality ($p=0.001$) but not respiratory mortality (possibly because of small no. of respiratory deaths (cf. CV or total deaths)) -O_x, temp. and NO_2 explained 4% of total mortality. -NO_2, CO, KM all correlated, but less strongly than temp, O_3 -statistical analysis appeared adequate, exhaustive. -TSP or PM_{10} not used; KM may be poor substitute (compare results of 1995 study where relationship of O_3 was attenuated to non-significance when PM_{10} was included in regression (Kinney et al. 1995)

Table 12.1a Ambient ozone and association with mortality

REFERENCE LOCATION TIME OF STUDY	OZONE, PPB	OTHER VARIABLES	STUDY DESIGN	RESULTS COMMENTS
Dockery et al. 1992 St. Louis, Mo. (pop. 2,356,000) 1 year, Sept 85-Aug 86 Kingston-Harriman, TN (pop. 641,000) 1 year, Sept 85-Aug 86	St. Louis 22.5 ± 18.5 (24-h mean, approx. equiv. mean of 1-h daily max. = 68) K-H, Tenn. 23.0 ± 11.4 (as above) 1 monitor in each site	~~St. Louis~~ (24-h means) PM_{10} 27.6 ug/m^3 SO_4 —8.0 ug/m^3 H^+ —9.7 nmole/m^3 SO_2—5.1 ppb NO_2—20 ppb deaths 20,449 (8.6/1000 person-y) ~~K-H, Tenn.~~ PM_{10} 30.0 ug/m^3 SO_4 8.7 ug/m^3 H^+ 36.1 n/mole/m^3 SO_2 5.1 ppb NO_2 12.6 ppb deaths 5670 (8.8/1000 person-years) temp., dew point temp., both locations	-daily deaths, excl. accidents, non-residents -Poisson regression -model included seasonal indicators, weather variables for same day and previous day	-Ozone not associated with mortality in St Louis ($p>0.3$) or in Tennessee -PM_{10} (a 100 ug/m^3 increase) was associated with a 16% increase in mortality in St. Louis, but did not reach statistical significance in Tennessee. -$PM_{2.5}$, SO_4, and H^+ had a weaker association with mortality in St. Louis -no gaseous pollutant was significant in St Louis -No association of mortality with any of the measured pollutants was observed in Kingston-Harriman, Tennessee -Since association of PM_{10} remained strong, despite a relatively low level, we conclude that if associated at all, ozone is a much weaker predictor than PM_{10} -No CO measurements or inclusion in regression -A seasonal indicator is too coarse to act as a filter for within-season variations in ozone and in mortality; this would also hide an association with a weaker variate such as ozone. -using a 24-h mean value reduces significance of ozone, since it occurs in high daily peaks with low concentrations at night (usually)
Kinney & Ozkaynak 1992 (abstract) New York City (pop. 8,000,000) 6 years, 1971-76	56 (mean of 1-h daily max.) (April-Sept only for O_3 - 36 months total)	CoH, SO_2, (values not given) Weather (temp. RH, visibility) deaths 163/d	-analysis was similar to their Los Angeles study (K&O 1991) -daily deaths, excluding accidents, suicides -daily cardiovascular and respiratory deaths -multiple regression analysis, using weighted 19-day filter for removal of seasonal trends in deaths and pollution variables	-Model including daily temp., RH, CoH (a measure of fine particles) and ozone (lagged 1 day) explained 10% of variation in total mortality -Slope of regression line for ozone was 0.55 deaths/ppb ($p<0.001$) -no details of monitoring were available (no. of stations, mean values, etc.) -analysis was thorough, based on statement that analysis was similar to LA (Kinney & Ozkaynak 1991) -CoH may be poor indicator of particulates; no SO_4 measurements

Table 12.1a Ambient ozone and association with mortality

REFERENCE LOCATION TIME OF STUDY	OZONE, PPB	OTHER VARIABLES	STUDY DESIGN	RESULTS COMMENTS
Li & Roth 1995 Philadelphia (pop. 1,642,000) 18 years, 1973-90	19.8 ± 14.4 (24-h mean, equiv. 1-h max. = approx. 60)	TSP 68.5 ug/m^3 SO_2 16.98 ppb ~~deaths~~ <65y ≥65y total 19.1/d 35.2/d cancer 5.7/d 7.8/d COPD 0.23/d 0.75/d card-v 5.2/d 17.6/d pneum. 0.38/d 1.31/d other 7.58/d 7.75/d	-daily deaths, except accidents -subdiv. by age, <65 y; ≥65 y -subdiv by cause: cancer, COPD, card.-vasc dis. (CV), pneumonia, other -compared a variety of stat models and methods -Poisson regression, incl. log transform & sq. root form -multiple regression -autoregression -smoothed out cyclic variations by trigonometric fit, terms for day of year filtered by unweighted moving averages gave only t-values	-Authors concluded that (I) effects of pollution on mortality are dependent on weather, and (ii) results are not consistent between models -Results appear to have reasonable internal consistency: O_3 signif. related to mortality for age ≥65, in 7 of 8 t-tests when TSP, SO_2 also incl. (8th test used only a 7-d moving average, too short) -O_3 not related to deaths for people <65 y in most tests -O_3 reduced correlation between TSP & deaths -TSP highly sign. by itself, but not with other pollutants -SO_2 signif. in 6/8 analyses, with TSP, O_3 included. -analyses did not include filtering for mortality data, also highly seasonal. -No CO, Nox in model -number of deaths too small for analysis in most subcategories -results agreed qualitatively with Moolkavgar study on Philadelphia
Moolkavgar et al. 1995 Philadelphia (pop. 1,642,000) 16 years, 1973-88	22.4, yearly av. (24-h mean, equiv. 1-h max = approx. 65-70) (summer) (spring) (fall) 11.9 (winter)	~~TSP, ug/m^3~~ 74 (su.) 210 max 67 (sp) 338 max 65 (fall) 215 max 66 (w) 205 max ~~SO_2, ppb~~ (su) 156 max (sp) 101 max (f) 100 max (w) 103 max ~~daily deaths~~ 54.3 (yearly mean) (51.0, 54.4, 52.6, 59.3; Su, Sp, F, W)	-daily deaths, except accidents and suicides (includes residents and commuters) -Poisson regression analysis -no evidence of autocorrelation -analysis by each 3-m season -correlation analysis of pairs of pollutants -treated each day separately in another model (may have acted as a kind of filter) -pollutants were lagged 1 day, combined with same day temp. -also analyzed entire year a single series with indicator variables for year, season, and quartile of temperature.	-ozone was assoc. with mortality in summer only (RR= 1.15, CI 1.07-1.24) when TSP, SO_2, weather incl. In model -When ozone was discretized into quintiles, only highest gave a pos. assoc. (>47.7 to 154 ppb) -SO_2 associated in spring, fall and winter (RR=1.19, 1.14, 1.21) -TSP not signif. If ozone included into model in summer, or SO_2 in other seasons -No CO in analysis -results showing O_3 most strongly related to mortality, followed by SO_2, agreed with Li & Roth (1995)

Table 12.1a Ambient ozone and association with mortality

REFERENCE LOCATION TIME OF STUDY	OZONE, PPB	OTHER VARIABLES	STUDY DESIGN	RESULTS COMMENTS
Kinney et al. 1995 Los Angeles Co. (pop. 7,901,000) 6 years, 1985-90 (only every 6th day for ozone, total 364 days)	70± 41 (1-h max.) range 3-201 8 monitoring sites (only used data for days when PM_{10} available, N= 364)	PM_{10}, ug/m^3 58± 23 (range 15-177) 4 sites, every 6th day (N= 364) CO, ppb 4.7±2.9 (range 1-13) 8 sites Weather- max. temp, mean RH deaths: 153±20/d	-daily deaths, excl. suicides, accidents, non-residents -the object was comparison of a range of statistical methods to derive RR for PM_{10} -OLS regression, log-linear anal., Poisson regression all tested (made little difference -cyclic data variations treated with dummy variables, season by season, 10-stage sine-cosine waves (couldn't use high-pass filter because had data for only every 6th day) -weather variables included -effects of other pollutants O_3 and CO tested with PM_{10}	-RR for O_3 only was 1.02 (1.00-1.05) when PM_{10} was included as a covariant, the RR for ozone was reduced to 1.00 (CI: 0.94-1.06). Ozone had no independent association with mortality; the data set for ozone was considered by the authors to be too small to draw any conclusions in view of expected weakness of association (N= 364 -RR of 1.05 for PM_{10} was unchanged when lag 1d O_3 and CO were included in the model -CO was also significant, with RR 1.05, same magnitude as PM_{10} (RR for PM_{10} reduced to 1.04 with CO in the regression)
Ozkaynak et al. 1995 (abstract) Toronto, Ont. (metro area) (pop. 3,000,000) 19 years, 1972-90	36 (mean of 1-h daily max.) (95th percentile approx. 66, Burnett et al. 1996)	Daily pollution data on TSP, SO_4, CoH, SO_2, CO, NO_2, from 16 monitoring stns. weather variables temp, RH. PM_{10} estim. from TSP Deaths 40/d	-daily plus cause-specific mortality, all ages categorized, for Metro Toronto -PM_{10} estimated from TSP data -multiple regression analysis including weather and air pollution variables -aggressive detrending of cyclic variations in both mortality and pollution data, using weighted 19-day linear filter -preliminary results only -preliminary results only	-Total estimated contribution of ozone plus particles to total daily mortality was approx. 3.8%, from model incl. temp, RH, same-day max O_3, TSP or PM_{10} -Ozone calc to contribute 1.5% and TSP 2.3% at the respective means (or 0.34% per 10 ppb of O_3 -slope for O_3 0.017 deaths/ppb -slope for TSP or PM_{10} 0.011/ug/m^3 (couldn't distinguish TSP from PM_{10})

Table 12.1a Ambient ozone and association with mortality

REFERENCE LOCATION TIME OF STUDY	OZONE, PPB	OTHER VARIABLES	STUDY DESIGN	RESULTS COMMENTS
Saldiva et al. 1995 Sao Paulo, Brazil (pop. 16,000,000) 1 year, May 90-Apr.91	38.5 (year), 17.7, (spr., sum.) (24-h means) (equiv. To approx. 36 as yearly mean of 1-h max) 38.3 max. year) 38.4 max. (spr, su) 4 monitoring stns	PM_{10} 82.4 ug/m^3 SO_2 6.5 ppb NOx 127 ppb CO 6.2 ppm PM_{10}, SO_2, CO at 8 monitoring stns., NOx at 3 stns. Deaths: 62.5/d (54.4/d in spr, sum.)	-daily mortality, persons >65y, within metro area -multiple and Poisson regression -controls, dummy variables for month of year, day of week, temp., rel. humidity -lagged moving averages of various lengths applied to air data (but not to mortality data) -autocorrelation adjustment -sensitivity analysis conducted	-Ozone (any measure) was not related to mortality when PM_{10} included as covariate -PM_{10} (100 ug/m^3 incr.) was assoc. with a 13% increase in mortality after inclusion of other covariates -linear relationship of quintiles from 45 to 130 ug/m^3, with RR=1 up to approx 60 ug/m^3 -assoc. of SO_2, NOx, CO disappeared after inclusion of PM_{10} in model (CO alone was stronger than PM_{10}) -Statistical analysis thorough, but mortality data unfiltered; makes difference in results obtained (Thurston & Kinney 1995) -Ozone levels were comparatively low while PM_{10} levels were very high; if both are involved in mortality increases, PM_{10} would act to obscure effect of ozone in this city.
Dockery et al. 1996 (abstract) Philadelphia (Pop. • 1,642,000) 1992-1993	N/A	$PM_{2.5}$, PM_{10}, SO_2 No data on values	-daily mortality, daily non trauma deaths-adjusted parametrically for trend, season, temperature and dew point -non parametric regression	-positive association between O_3 (0.9% increase in death for every 10µg/m^3 increase in O_3)—independent and additive to the $PM_{2.5}$ associations. O_3 was not consistent by season, since RR was lowest in summer. -association between daily non trauma deaths and $PM_{2.5}$ concentrations of the previous day (2% increase in death associated to 10µg/m^3 increase in $PM_{2.5}$ and to a lesser degree with PM_{10} (1.2% for 10µg/m^3 PM_{10}) -no association with coarse particles, total aerosol acidity, SO_2 and negative association with CO
Ito and Thurston 1996 Cook County (Chicago) (pop. 5.3 million in 1986) 1985-1990	38 ± 19.9 6 year average, 5 sites, average of all sites, missing data regressed from other sites	PM_{10} 40.7 ± 19.1 µg/m^3, CO 2.05 ± 0.95 ppm, SO_2 24.5 ± 14.7 ppb, Weather (T, RH, Bar. Pres., wind speed, B[illegible])	-daily mortality (two race categories: black and white, 3 age categories: 15-60, 60+ and all ages, male and female) -five death categories: total deaths excluding injury and poisoning, circulatory, respiratory, cancer and residual (total minus circulatory-respiratory-cancer) -Poisson regression or a log-linear Generalized Linear Model -adjusted for temperature, time-trend, day of week (dummy variables), long-wave cycles	-positive association between O_3 and total mortality with both single and two-pollutant models (RR=1.10; CI: 1.06-1.15 and RR=1.07; CI: 1.01-1.12 per 100 ppb increase of O_3 respectively) -positive associations were found also between O_3 and circulatory or cancer deaths, but not for respiratory or residual mortality (RR• 1.13; CI: 1.06-1.2, 1.09; CI: 0.99-1.18, 1.1; CI: 0.95-1.28, and 1.08; CI: 0.98-1.2 per 100 ppb of O_3 respectively) -correlation of PM_{10} and O_3 coefficients was -0.37, higher correlation between O_3 and T than PM_{10} and T, suggesting some degree of sharing of effects between PM_{10} and O_3, and O_3 and temperature -PM_{10} was associated with total, cancer, and respiratory mortality but not with circulatory or residual mortality (RR=1.05; CI: 1.03-1.08, 1.12; CI: 1.06-1.18, 1.14; CI: 1.04-1.25, 1.03; CI: 0.98-1.07, and 1.01; CI: 0.95-1.08 per 100 µg/m^3 PM_{10} respectively)

Table 12.1a Ambient ozone and association with mortality

REFERENCE LOCATION TIME OF STUDY	OZONE, PPB	OTHER VARIABLES	STUDY DESIGN	RESULTS COMMENTS
Anderson et al. 1996 London (England) April 1987 - March 1992	15.5 ± 10.9 (8 h average) 20.6 ± 13.2 (1 h maximum) Single background monitor	BS (black smoke): 14.6 ± 7.0 $\mu g/m^3$ (24h average) NO_2 37.2 ± 12.3 ppb (24 h average), 57.2 ± 23.0 ppb (1h max.) SO_2 32.0 ± 11.7 $\mu g/m^3$ (24h average) Temperature, Relative Humidity	-Poisson regression analysis of daily counts of deaths with adjustment for effects of secular trend, seasonal and other cyclical factors, day of week, holiday, influenza epidemic, temperature, humidity, and autocorrelation (lagged 0-3 days) -RR of death from all causes (excluding accidents), respiratory disease, and cardiovascular disease.	-positive association between O_3 and increase in all cause, cardiovascular, and respiratory mortality (same day) with greater effects in warm season -O_3 effects independent of other pollutants -during warm season, increase of 8 h O_3 concentration from 10th percentile to 90th percentile of the seasonal range (7-36 ppb) was associated RR=1.0348; 95% CI:1.0173-1.0526, RR=1.0355; CI: 1.0104-1.0613, RR=1.0541; CI: 1.0035-1.1073 respectively for all cause, cardiovascular and respiratory mortality - similar results of positive associations between O_3 and mortality were observed for 1 h maximum all year and warm season data -positive association between PM_{10} and all cause mortality (lag one day), independent of other pollutants, significant for all year, warm and cool season, but greater effect in warm season(RR= 1.0245; CI: 1.0088-1.0405 for warm season)
Sunyer et al. 1996 Barcelona (Spain) 1985-1991	28.1 (3.6-96.4)[2] in winter (w) 44.1 (4.8-144.4) in summer (s) 1h maximum	BS w=49.7$\mu g/m^3$ (11.4-66.7); s=35 $\mu g/m^3$ (10.6-125.6) 24h mean SO_2 w=46 $\mu g/m^3$ (2.2-160); s=36.4 (5.4-116.5) 24h mean NO_2 w=88.4 $\mu g/m^3$ (8.3-339.2); s=97.3 (8-336.4) Temperature, Relative Humidity,	-Autoregressive Poisson regression model analysis of daily variation in total mortality, mortality in subjects >70 years, and cardiovascular and respiratory mortality; -control for temperature, relative humidity, influenza epidemic, seasonality, day of week, holidays, long term trends	-positive association between O_3 and total mortality (lag 0), mortality • 70 years (lag 1), cardiovascular mortality (cv) (lag1) for both all year (ay) and summer data (s) but not for winter (w): Total mortality (95%CI) RR: ay=1.048;(1.012-1.086), s=1.058; (1.017-1.101), Elderly mortality ay=1.042; (1.003-1.082), s=1.059; (1.016-1.105), cv mortality ay=1.058; (1.009-1.111), s=1.088; (1.028-1.152), correlation coefficient –0.33 (BS) to 0.3 (NO_2) -also positive associations between NO_2 and total mortality (lag1), mortality • 70y (lag 1), and cardiovascular (lag 1) for ay, s but not w -strongest associations between SO_2 and total mortality (lag1), mortality • 70y (lag 1), and cardiovascular (lag 1) for ay, s and w and also for summer and respiratory mortality (lag 0) -also strong associations between particles (BS) and total mortality (lag1), mortality >70y (lag 1), and cardiovascular (lag 1) for ay, w but not s, and possibly significant for ay & w for respiratory mortality (lag3) -all data are RR per 100 $\mu g/m^3$ increase in air pollutant

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[2] Data provided in $\mu g/m^3$ and transformed in ppb

Table 12.1a Ambient ozone and association with mortality

REFERENCE LOCATION TIME OF STUDY	OZONE, PPB	OTHER VARIABLES	STUDY DESIGN	RESULTS COMMENTS
Verhoeff et al. 1996 Amsterdam (pop. 716,000 in 1992) 1986-1992	21.9[3] (1h max.; percentiles:10 %=4.1, 25%=10.2, 50%=19.9, 75%=30.1, 90%=41.3, maximum value=153.3	BS=12 µg/m^3 (max=81) PM_{10}=38 µg/m^3 (max=163) SO_2=13 µg/m^3 (max=139) CO= 973µg/m^3 (max=9057) Temperature, Relative Humidity,	-Poisson regression analysis of total mortality and age stratified mortality (Municipal population register--no data on cause of death) study may be bias because of this oversight -control for seasonal and long-term temporal patterns (year of study, month, day of the week, epidemic of influenza-type illnesses, weather terms) -current day, lag 1, 2 days data	-positive association between O_3 and total mortality (lag 2 d), single pollutant model: RR=1.049 (95% CI: 1.001-1.100) for 100 µg/m^3 increase (or 50 ppb), or RR=1.098 (CI:1.002-1.200) for 100 ppb increase. -positive association between BS and total mortality with one pollutant (current day) RR=1.187; CI: 1.020-1.380, and two pollutant models +SO_2-RR=1.265; CI: 1.073-1, +CO-RR=1.203; CI: 1.005-1.441, +O_3-RR=1.178; CI: 1.011-1.373 - inclusion of O_3 and BS together reduced RR of O_3 to 1.029 (CI: 0.967-1.096) per 50 ppb increase, while BS remained stable; -inclusion of O_3 and PM_{10} together in the model reduced the RR of each pollutant. Ozone RR=1.050 (CI: 0.947-1.165) per 50 ppb increase. - warm season (May – October) RR for ozone (single-variate model) was 1.04 (95%CI 0.99-1.09) per 50 ppb. -Mortality data: accidental death included
Zmirou et al.1996 Lyon (France) pop. 410,000 1985-1990	7.75 (0-77) (1h max.) 5.1 (0-40.2) (8-h mean) One site (urban centre)	SO_2 (5 sites)24h mean=46.76 (2.16-314.57); 1 h max. 100.22 (4.71-635.69) PM_{13} (3 sites) 24h mean 38.05 (2.67-179.81) NO_2 (1 site) 24h mean = 70.17 (3.50-323.75); 1h max. 132.73 (9.55-737.26) Temperature, Relative Humidity	-Poisson regression of total mortality (accidental deaths excluded), respiratory, cardiovascular and digestive causes (control) controlling for best fit time patterns and weather factors (trends, day of week, holiday, temperature, humidity, autocorrelation)	-no association between mortality and O_3; RR (1-h max.)=1.16 (95% CI: 0.76-1.64); RR (8-h mean)= 1.12 -only one site for O_3 monitoring in urban centre, potential scavenging, may not reflect actual population exposure -ozone concentrations very low, + number of deaths/day also low, leading to instability on results -SO_2 is the only pollutant that shows a clear association with mortality in the city of Lyon (total, respiratory, cardiovascular) -PM_{13} was associated with cardiovascular and respiratory mortality (marginal for cv mortality) -no association was found between any of the pollutants and digestive mortality (control) (0.80-1.48).

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[3] Data provided in µg/m^3 and transformed in ppb.

Table 12.1a Ambient ozone and association with mortality

REFERENCE LOCATION TIME OF STUDY	OZONE, PPB	OTHER VARIABLES	STUDY DESIGN	RESULTS COMMENTS
Ostro et al. 1996 Santiago, Chile (pop. 4.4 million) 1989-1991	1h (max.) 52.8 ppb (11-264)	PM_{10} 24h mean: 112.9 (32-336), 119.5 (30-367), 113.4 (35-308) µg/m^3 respectively for each year; daily max: 147.2 (35-500), 143.5 (35-424), 132.9 (39-340) NO_2 1h max. 55.6 (10-258) ppb SO_2 1h max. 59.9 (4-363) ppb Temperature, Relative Humidity	Poisson regression of specific mortality, and least square regression and parametric tests were used for total mortality (results from both distribution techniques are reported) controlling for temperature, month, season, day of the week	-positive association between total mortality and O_3 for summer months only using both methods (RR=1.02; CI: 1.00-1.05 and RR=1.04; CI: 1.00-1.09 per 100 ppb using least square and Poisson regression respectively) -O_3 was well correlated with max. temperature (r=0.68) and to a lesser degree with min. temperature (r=0.42) -positive association between PM_{10} and mortality (total, specific, age stratified)--association remained significant all two pollutant models -authors conclude that O_3 may have an independent effect on mortality as it had a stronger association with mortality (based on p-value) than did PM_{10}
Dab et al. 1996 Paris France (pop. 6.1 million) 1987-1992	22.3 (3-75) 5th-95th%(1-h max.) 14.1 (10-56)(8-h mean) (5th-95th)	SO_2 29.7 (24-h) 59.9 (1-h) BS 31.9 (24-h) PM_{13} 50.8 (24-h) NO_2 45.0 (24-h) 73.8 (1-h)(all Fg/m^3)	Poisson autoregression models Respiratory mortality only Controls for best fit models including long term trends, seasonal, weekly + daily patterns, holidays, influenza epidemics and weather (temperature, humidity)	The ozone RR for respiratory deaths was elevated, but 95% confidence limits were wide and included the null value. RR 1.16 (95% CI 0.87-1.62) (1-h max, 100 ppb increase) RR 1.29 (95% CI 0.87-1.94) (8-h mean, 100 ppb)
Touloumi et al. 1997 6 APHEA cities 3 additional cities	Athens 48 Barcelona 37 Koln (no data) London 21 Lyon 7.6 Paris 23 Amsterdam 22 Basle (not given Zurich (A ●)	 BS 84.4 NO_2 135 (µg/m^3) BS 46.6 NO_2 97.8 BS 14.6 NO_2 109.4 BS 31.6 NO_2 70.1	Data were analysed by each city separately following a standardised methodology to ensure comparability of results. Poisson autoregressive models were used for control of seasons, temperature, humidity, and influenza epidemics. Fixed effects models were used to pool the individual regression coefficients when there was no evidence of heterogeneity among the cities and random effects models otherwise. For meta-analysis, Amsterdam, Basel, Geneva and Zurich were added.	-Positive associations between daily deaths and NO_2 and ozone. Increases in 50 µg/m^3 in NO_2 (1-hr max.) or 25 ppb ozone (1-hr max.) were associated with a 1.3% (95% CI 0.9 – 1.8%) and 2.9% (95% CI 1.0- 1.9%) increase in the daily number of deaths, respectively. - RR of ozone in the model including NO_2 was 3.2% (95% CI – 0.3 to 6.8%). RR of NO_2 in the model including ozone was 1.5% (95% CI 0.9 to 2.0%). Stratified analysis of NO_2 effects by low and high levels of black smoke or ozone showed no significant evidence for an interaction within each city. -The pooled estimate of RR for ozone effect was slightly reduced [2.8% (95%CI 0.5 to 5.0%)], whereas the one for NO_2 was almost halved but remained significant[0.6% (95%CI 0 to 1.2%)], when two pollutant models including black smoke were applied.

Table 12.1a Ambient ozone and association with mortality

REFERENCE LOCATION TIME OF STUDY	OZONE, PPB	OTHER VARIABLES	STUDY DESIGN	RESULTS COMMENTS
Loomis et al., 1996 Mexico City (5 sub-areas) 1990-1992 3 years, 1990-1992	O_3 daily 1-h maximum: 154 ppb (range 26-319 ppb) The 1-h max. value of ozone was above 120 ppb, approximately 75% of the days. O_3 24-h mean: 62 ppb (range 12 -130 ppb)	TSP: every 6 th day as a 24-h mean: 168 μg/m^3 (86-460 μg/m^3) SO_2 as an 24-h mean: 54 ppb (9-135 ppb) Also monitored: temperature (daily minimum and maximum, daily average and difference between min. and max.) 9 monitoring stations Total deaths: 31/d	-Number of daily deaths in the 5 sub-areas -Deaths were grouped by age (<5yr, 5-64y, ≥65y) and causes (respiratory diseases, cardiovascular diseases, accidents and other causes) -Poisson regression analysis (controlling for potentially confounding covariates: temperature, periodic phenomena related to the year, the months, the day of the week and holidays -Same day and lagged 1 day checked -Temperature indices with lags of one to nine days were tested	When reviewed only single pollutants in the statistical model: -daily deaths increased 5.4% for each 100 μg/m^3 increase in TSP -daily deaths increases 7.5% for each 100 ppb increase in SO_2 -daily deaths increased 2.9% for each 100 ppb increase in O_3 (RR=1.029, 95% CI= 1.015-1.044) (this excess mortality was greater for people aged ≥65 years) -When O_3, TSP and SO_2 were included in the model, only the association with TSP with the observed increase in daily mortality was statistically significant [RR=1.052 (95% CI= 1.034-1.072)] -Bivariate of O_3 and SO_2 not given

Table 12.1a Ambient ozone and association with mortality

REFERENCE LOCATION TIME OF STUDY	OZONE, PPB	OTHER VARIABLES	STUDY DESIGN	RESULTS COMMENTS
Kelsall et al., 1997; Samet et al., 1997 Philadelphia, PA 15 years, 1974-1988	O_3 24-h mean 19.8 ± 14.6 ppb 8.3-28.5 IQR (=20.2)	Other pollutants were measured over a 24-h period (mean): TSP: 37.3 µg/m^3 SO_2: 17.3 ppb NO_2: 39.6 ppb CO: 17.4 ppb (x100) Total deaths: 46.7/d Respiratory: 2.5/d Cardiovascular: 20.2/d Other 24.0/d	-Number of deaths of Philadelphia residents (mortality data were stratified by age (<64y, 65-74y, ≥75y) and causes of deaths (respiratory, cardiovascular and others) -Estimation of the percentage change in daily mortality per interquartile change in each of the air quality variables, controlling for day of the week and long-term and weather-related trends -Poisson regression analysis with fitting generalized additive models (GAM) -Study of the effect of each pollutant individually (with controlling for time trends, season and weather) and then in pairs and finally all pollutants together	-O_3 was weakly correlated with the concentrations of other pollutants -Mortality significantly increased with increasing TSP, and O_3. -1.1% increase in mean mortality attributable to a 10 ppb increase in mean daily ozone in univariate analysis (2% increase for 20.2 ppb ozone). -TSP remained statistically significant in the model along with O_3 -When TSP and SO_2 considered together: their effect dropped by approximately 40% -O_3, TSP, SO_2, NO_2 and CO together: significant effects of SO_2 and O_3 -TSP effect was strongest in spring and summer and O_3 effect was greatest in winter and fall -TSP effect tended to be greatest in the oldest category (≥75y) - O_3 effect was positive across all cause-of-deaths categories with no consistent variation by age groups -Results agreed with Moolkavgar and Li & Roth studies

Table 12.1a Ambient ozone and association with mortality

REFERENCE LOCATION TIME OF STUDY	OZONE, PPB	OTHER VARIABLES	STUDY DESIGN	RESULTS COMMENTS
Wietlisbach et al., 1996 Zurich, Basle and Geneva, Switzerland, 1984 – 1989.	Mean ± SD (presumably 24-h average), μg/m^3: Zurich: 26.9 ± 21.0; Basle: 23.9 ± 19.4; Geneva: 0	Total mortality, mortality for people >65 y, respiratory mortality, cardiovascular mortality. TSP, SO_2, NO_2, CO, temperature, RH	1. Standard Poisson regression model to evaluate time trends, seasons and weather variables (temperature and RH) alone with pollutants. 2. Semi- and fully-nonparametric Poisson models, locally weighted regression smoothing. Data reported using this model. 3. Gaussian regression models; co-variates in the models.	• Association of mortality with ozone was weak and inconsistent. • Mortality was associated with TSP, SO_2, and NO_2. • When all five pollutants were in the model, regression coefficients on the pollutants were unstable and statistically insignificant: -For total mortality, regression coefficient (± SE) for Zurich was 0.012 (0.027), for Basle 0.075 (0.074), and no data for Geneva. -For mortality of people >65 years of age, regression coefficient (± SE) for Zurich was 0.005 (0.030), for Basle 0.145 (0.083, $p<0.05$), and no data for Geneva. -For respiratory mortality, regression coefficient (± SE) for Zurich was -0.151 (0.067, $p<0.05$), for Basle 0.193 (0.155), and no data for Geneva. -For cardiac mortality, regression coefficient (± SE) for Zurich was –0.003 (0.040), for Basle –0.163 (0.116), and no data for Geneva
Burnett et al., 1998 Canada (11 cities) (pop. 10,800,000) 12 years (4383 days), 1980-1991	O_3 24-h average of 11 cities: 16.2 ppb Data were averaged over all monitoring stations in each city (data not given)	Monitored as an 24-h period (mean): NO_2: 23.5 ppb SO_2: 5.4 ppb CO: 1.0 ppm Also monitored: daily 1-h maximum and minimum temperature, daily average dew point and relative humidity Non-accidental deaths: 816 991 deaths; 196.5/d	-Number of daily deaths for non-accidental causes: (ICD-9, codes 1-799) -Multiple regression analysis, using a 19-weighted linear filter to remove city-specific long term trends, seasonal, sub-seasonal, day of study, day of the week effects and weather	-Day to day variations in O_3 were negatively correlated with NO_2, SO_2 and CO -CO and NO_2 were highly correlated; NO_2 and SO_2 were also positively correlated, CO and SO_2 were positively associated too. -Based on a single pollutant model, a 0.9% ($p\leq0.05$) increase in mortality was associated with a 10 ppb increase in 24-h mean O_3 -NO_2 had the largest effect on mortality with a 4.1% increased risk ($p<0.01$) follow ed by O_3 at 1.8% ($p<0.01$), SO_2 at 1.4% ($p<0.01$) and CO at 0.9% ($p=0.04$). in a multiple pollutant regression models. -All pollutants together: association of 8.2% of premature deaths -$NO_2 > O_3 > SO_2 >$ CO -When cities were analyzed separately: 24-h O_3 was a significant predictor of mortality in 6 cities

12.2.1 Studies reporting significantly positive associations between ozone and mortality

Seventeen of the 23 mortality studies reported statistically significant positive associations between increases in mortality and ground level ozone pollution, using single- or multiple-pollutant models. These associations could not usually be explained on the basis of yearly trends, day-to-day variations, epidemics, or weather. The latter is the most important source of variation with respect to the ozone-mortality association because ozone is often correlated with temperature in summer, while both minimum and maximum temperatures have also been associated with increased mortality. All studies adjusted temperature and relative humidity in some way in their regressions, and also included other cyclic factors that were shown to influence the results during preliminary analyses. These associations were found in cities across North America, in 4 U.S. and 13 Canadian locations, in Santiago Chile and three European cities, and in a meta-analysis including seven European cities, demonstrating consistency of results despite widely varying climatic conditions and pollutant mixtures.

These associations were reported for cities with mean ozone concentrations (reported as the one-hour maximum) between 20 and 75 ppb, i.e. below, and in most cases well below the current Canadian objective for ozone of 82 ppb. However, some lack of predictability using this criterion alone was noted due to negative results in several cities with mean concentrations from 22 ppb [Paris (Dab et al., 1996), Amsterdam (Verhoeff et al., 1996)] to as high as 154 ppb in Mexico City.

Twelve of these studies with significant results provided quantitative estimates of risk based on regressions including ozone as the only air pollutant in the model, adjusted for weather, season and other cyclic variables. The relative risks (RR) for all-cause mortality (excluding accidents in many studies) varied between 0.24% and 1.16% per 10 ppb increase in ozone, measured as the 1-hour maximum. The mean RR (from studies with significant results, n=12) was an increase in daily mortality of 0.65% (standard deviation 0.36%) per 10 ppb increase in ozone, and the median was 0.53%. The multi-pollutant analysis data will be discussed in Section 12.2.3.

In terms of the impact of particulate matter on the association between ozone and mortality, in Los Angeles (Kinney & Ozkaynak, 1991) and New York (Kinney & Ozkaynak, 1992), the particulate pollution did not have a completely satisfactory surrogate. KM (an optical measurement) was used in Los Angeles while COH (another optical reading of carbonaceous soot) was used in New York (no sulphate measurements were given in either location). Particulate matter was not strongly associated with mortality in either location, and the possibility exists that at least some of the relationship seen with ozone could have been due to particulate matter. In a later analysis of pollution data from Los Angeles (1985-90), in which PM_{10} measurements were available, ozone was not found to be related to mortality after inclusion of PM_{10}. The authors cautioned that too few co-occurring data points were available (n=364) to separate their effects (Kinney et al., 1995). In Toronto, the small but significant relationship of ozone (estimated to account for 1.5% of additional mortality at 36 ppb) and the somewhat stronger association of TSP and PM_{10} (2.3%) to daily mortality (at 42 ug/m^3 PM_{10}) may be a reasonably accurate reflection of the true relationship between these two pollutants and daily mortality in this location (Ozkaynak et al., 1995). Ozone was relatively lower than in Los Angeles (36 ppb, mean of 1-h daily max.); daily TSP and sulphate measurements were available, and PM_{10} was estimated from these.

Li and Roth (1995), Moolkavgar et al. (1995), Samet et al. (1997) and Kelsall (1997) all looked at data from Philadelphia which were extensions and reanalyses of data from earlier studies (Shumway et al., 1988; Schwartz & Dockery, 1992) showing a relationship of TSP to daily mortality. Li and Roth (1995) were most interested in testing a wide variety of statistical models for comparison purposes, and presented only t-values for TSP, SO_2, and ozone, showing considerable model-dependent variability. In the summer only, ozone was significantly associated with mortality in people over age 65, in 7 of 8 models, with t-values ranging from 2.8 to 3.8 for 6 of the 7 positive tests (the seventh was highly significant at 5.8). The first two studies were remarkably consistent (considering differences in methodology) in finding ozone to be most strongly related to mortality, with SO_2 also related, although less strongly, and in finding the association between TSP and mortality to be insignificant after ozone and SO_2 were included in the analysis.

The study by Moolkavgar et al. (1995) treated each day of the year separately (18 years), and used indicator variables in their regression for year, season, and temperature. The reason for the lack of significance of TSP in Philadelphia was unclear. The recent extensive re-analysis of the Philadelphia data by the Health Effects Institute (Samet et al., 1997, Kelsall et al., 1997) confirmed that ozone was an important element of the air pollution mixture associated with mortality in Philadelphia. There was an estimated 1.1% increase in mean mortality attributable to a 10 ppb increase in mean daily ozone in univariate analysis and also 1.0% in a multipollutant analysis that included all five "criteria" pollutants. The coefficients for TSP and SO_2 were about half that for ozone, while NO_2 and CO were not found to have a positive association in univariate analyses, thus confirming the previous Philadelphia findings on the role of O_3 and SO_2 , but adding TSP as an important predictor of mortality. The reversal of the roles of NO_2 and TSP in the bivariate regression is a reflection of the high correlation coefficient between these pollutants.

Subdivision of total deaths into respiratory and cardiovascular causes was investigated by Kinney & Ozkaynak (1991) for Los Angeles. Oxidants (mostly ozone) were associated with total and cardiovascular deaths, but not with respiratory deaths, contrary to expectations based on morbidity studies and clinical studies in which the only effects were respiratory in nature. However, the number of respiratory deaths per day (8) was very low, and was less than one-tenth the cardiovascular deaths (87/day), quite possibly accounting for the observed lack of association with respiratory deaths.

More recently, studies by Dockery et al.(1996), Ito and Thurston (1996), Loomis et al. (1996), Sunyer et al.(1996), Anderson et al.(1996), Verhoeff et al.(1996), Ostro et al. (1996), Touloumi et al. (1997), Kelsall et al. (1997), Samet et al., (1997), and Burnett et al. (1998), examined 7 cities plus two groups of cities (one in Europe and one in Canada) and found positive associations between ozone and total mortality.

Dockery et al. (1996) is only an abstract with limited information on ozone. The authors state that there is a specific effect of fine particles (PM_{10} and $PM_{2.5}$) with a possible additional effect of ozone. A 0.9% increase in mortality per 10 ppb ozone was estimated in a bivariate regression including $PM_{2.5}$, which remained significantly associated with mortality. The association of ozone with mortality is considered to be independent and additive to the $PM_{2.5}$ association.

Ito and Thurston (1996) looked mainly at the association of PM_{10} and mortality. Three categories of deaths (cancer, respiratory, circulatory) plus total non-accidental and residual deaths (total minus the three categories) were included in the data. It was found that both PM_{10} and ozone were associated with increases in total and cancer mortality (using single and two-pollutant models). A 1% increase in total non-accidental mortality was predicted for a 10 ppb increase of O_3; this estimate was reduced to a 0.7% increase (95% CI: 0.1-1.2%) when PM_{10} was included in a bivariate regression. Respiratory mortality was associated only with PM_{10} and circulatory mortality only with ozone. The total number of deaths per day was 9.8 for respiratory causes this resulted in a larger standard deviation (SD) than that for circulatory causes, which might explain the lack of significance for ozone. The authors stated that the relative risk (RR) were more uniform among the categories for ozone when compared to PM_{10}. The interpretation of the results for PM_{10} and breakdown by race, gender and cause specificity were not conclusive because of large standard errors for these small-count sub-categories. The authors concluded that in this study, both ozone and temperature showed no cause-specificity, while PM_{10} was more cause-specific for respiratory and cancer deaths. The authors also suggested that some residual confounding of the ozone results by temperature may have occurred.

A study on a second large Latin America city, Mexico City (Loomis et al., 1996), demonstrated a very small positive association between O_3 and mortality, with a 0.24% (95% CI 0.1-0.4%) increase in mortality per 10 ppb increase in ozone, measured at the 1-hour maximum. Ozone related mortality was increased for the elderly, aged $\geq$65y, and for cardiovascular disease (CVD), but not for respiratory diseases, possibly because of low numbers of deaths from respiratory diseases (3/day) compared to death from CVD. PM_{10} was a much more important predictor of mortality than ozone in this location, and bivariate analysis including both pollutants resulted in loss of association between O_3 and mortality. Further discussion of these results follows in section 12.2.3.

In the study by Sunyer et al., (1996) in Barcelona, a 10 ppb increase in ozone (1-h max) was associated with a 0.96% increase in mortality (95% CI 0.24-1.72%), and the risk was increased to 1.16% when summer months only were included. In this study, SO_2 was the pollutant that was most highly associated with mortality (all categories except respiratory) and the only one associated with respiratory mortality. RRs for this pollutant were all higher than for any of the other pollutants. No co-regressions with combination of pollutants were performed because of high colinearities between pollutants. It is, therefore, impossible to determine if the effects attributed to ozone were truly independent of other pollutants. The interaction between pollutants and season were assessed. Some correlation was found between the following pollutants and physical variables: between ozone and temperature (r=0.415), PM_{10} and SO_2 (r=0.634), PM_{10} and ozone (r=-0.334).

Only one monitor was used for ozone in the Anderson et al. (1996) study in London (UK), which may not properly reflect the levels in London because of its central urban location and greater probability for scavenging effect, and may have caused misclassification of exposure. A positive association was found between ozone and total mortality, as well as cardiovascular mortality and respiratory mortality. These effects were greater during the warm season. The ozone effects were also independent of other pollutants, particularly British Smoke Shade (BS), which was not found to be associated with mortality after accounting for the ozone effect.

In the study by Verhoeff et al. (1996), the authors used the Municipal Population Registry which does not provide the cause of death. This limitation in the study may have introduced a slight bias since information on accidental deaths is included in the mortality data (accidental deaths were roughly five percent of total deaths). The study found a positive association between ozone and total mortality, with an estimated 0.98% increase in premature deaths per 10 ppb increase in O_3

(95% CI 0.02-2.0). In bivariate regressions with BS or PM_{10}, the confidence limits of the regression coefficient for O_3 were broadened and included the null value. The study is nonetheless considered to provide support for the association of ozone with mortality for the reasons outlined in section 12.2.3.

Ostro et al. (1996) used two different regression models, the Poisson model and the ordinary least squares (OLS) model, to study the association of mortality and pollutants in Santiago, Chile. When applied to ozone, both models demonstrated a significant association with total mortality only during the summer months with an estimated 0.4% (95% CI 0.0%-1.0%) increase for each 10 ppb increase in O_3 in single-pollutant analysis (Poisson model, 0.2% increase from OLS model). The authors concluded that ozone may have an independent effect on mortality, as ozone correlated weakly with PM_{10}, NO_2 and SO_2 (r was –0.23, -0.06 and 0.00, respectively), and ozone retained its significant association with mortality when both PM_{10} and ozone were included in bivariate analyses.

In the recently published European APHEA (Air Pollution and Health – A European Approach) study (Touloumi et al., 1997), six cities (Athens, Barcelona, Koln, London, Lyon and Paris) spanning Central and Western Europe, were examined. The mean of the hourly maximum of ozone varied from 93.8 ppb in Athens to 15.2 ppb in Lyon. Particulate pollution was measured as BS. The data were analyzed by each center separately following a standardized methodology to ensure comparability of results. Poisson autoregressive models allowing for overdispersion were fitted to remove seasonal and long-term trends from the mortality series, day of the week patterns, local characteristics such as holidays, and influenza epidemics. Meta-analyses were conducted using fixed effects models to pool the individual regression coefficients when there was no evidence of heterogeneity among the cities, and using random effects models otherwise. Data reported a significant association between daily mortality and ozone levels, and nitrogen dioxide as well. Stratified analysis of nitrogen dioxide effects by low and high levels of BS or ozone showed no significant evidence for an interaction within each city. The association was such that the authors concluded that an increase of 50 $\mu g/m^3$ (25 ppb) in ozone for the hourly maximum would result in a 2.9% increase in the number of deaths from all causes.

The authors (Touloumi et al., 1997) further conducted a meta-analysis adding four more European cities (Amsterdam, Basle, Geneva and Zurich), which resulted in a virtually identical estimate. It is of interest to note that the risk estimates for the cities of Paris, Amsterdam, Zurich and Basle were of marginal significance when considered individually, but treatment as a unit narrowed the confidence limits and increased the statistical significance. These two groups of cities were admirable candidates for meta-analysis because they all used similar protocols.

Burnett et al. (1998) have shown a positive association between O_3 and total non-accidental mortality in 11 Canadian cities. Based on a single pollutant model, a 0.86% ($p \leq 0.05$) increase in mortality was associated with a 10 ppb increase in 24-h mean ozone, in the 11 cities considered together (population 10.8 million studied over the 12-year period 1980-1991). NO_2 had the highest contribution to the air pollution effect on mortality (5.3% for a 23.5 ppb mean increase) followed by CO (2.5%) and SO_2 (1.8%) for 1 ppm and 5.4 ppb mean increases respectively. When all gaseous pollutants were included simultaneously, it was estimated that a total of 8.2% premature deaths were associated with the gaseous air pollutants, of which ozone contributes approximately one-fifth, NO_2 one-half, SO_2 one sixth, (all at $p \leq 0.01$) and CO one tenth ($p \leq 0.05$). When individual cities were analyzed separately, 24-h ozone was a significant predictor of mortality in 6 of the eleven cities.

Two potential problems with this study concern the lack of data on particulate matter and its effect on the risk estimates, and the problems created by including moderately or highly collinear pollutants together in multivariate analysis. In a previous paper on hospitalization data by the same group of authors (Burnett et al., 1997a) the entire air pollution effect was claimed to be explained by a combination of the gaseous pollutants, with no additional increase in model fit after adding particulate matter. The present paper attributes about an additional 1% to particles (+8% from the gases) in a separate analysis of the effect of reduction of sulphur in gasoline on mortality in 5 of the 11 cities.

The problem of collinearity appears to be a reasonable explanation of the inconsistency of effects of ozone and other pollutants, in individual cities. Although the average correlation coefficients were low or low-moderate ($r \leq 0.35$), they were much higher in some cities (e.g. $r=0.7$ for NO_2-CO in Edmonton).

In an analysis conducted for the Working Group on Air Quality Objectives and Guidelines (WGAQOG) of CEPA/FPAC, Burnett (1998) expanded the 11-city analysis to 13 cities, including Halifax and St-John to represent the Atlantic Region. In this case, 1-hour maximum ozone was used to examine the relationship between ozone and non-accidental mortality. Both the mortality data and the daily variations in 1-hour maximum ozone levels were adjusted using pre-filtered non-parametric smoothed functions of day of study and day of week differences for each city, which also acted to normalize data among cities. City-specific weather effects were also removed by adjusting temperature, daily average dew point temperature, and average relative humidity in non-parametric smoothed functions. Current day, and lag one to 4 days were considered. (See Appendix A for detailed methodology and results).

Data from this analysis (Burnett, 1998) demonstrate that the risk of premature mortality attributable to a 10 ppb increase in (1-h maximum) ozone was 0.79% (95% CI: 0.59-0.99%) for current day exposure (lag 0 d) and 0.65 ± 0.11% for the previous day exposure (lag 1 d). The risk decreased for each successive lag day, and the confidence intervals included the null value for lag days 3 and 4. The results were obtained using the combined data from the 13 cities, in order to utilize information from all regions of the country as well as to increase statistical power. The concentration-response curve appeared to be linear (not shown). A sensitivity analysis was undertaken to find the lowest ambient ozone concentration that could be statistically associated with mortality, by progressively removing days when the concentration was above 50, 45, 40, 35, 30, 25, 20, 15, and 10 ppb, respectively. The risk remained essentially constant (0.77 to 0.92% per 10 ppb increase) for all concentrations at 20 ppb and above, at the 99% confidence level ($p<0.01$. There was no evidence for a threshold in the mortality data. A difficulty with this analysis is the lack of accounting for the potentially confounding effect of other air pollutants. However, a similar analysis with most of the same data set demonstrated that CO, NO_2, and SO_2 did not confound the effect of ozone on mortality (Burnett et al., 1998). Fine particles are also a possibility for confounding effects, but daily measures of particulate mass were not available for the 13 cities in this analysis. Since ozone and fine particles are not correlated when the entire year is examined, and since fine mass (as sulphates) did not confound this association between ozone and hospitalization in Southern Ontario (Burnett et al., 1994, 1995), this provides some assurance that ozone acts independently in its effects on mortality in the Burnett (1998) analysis.

12.2.2 Studies reporting non-significant associations between ozone and mortality

In six studies (7 locations), no significant relationship of ozone to mortality was found (Schwartz, 1991; Dockery et al., 1992; Saldiva et al., 1995; Zmirou et al., 1996; Dab et al., 1996 and Wietlisbach et al. (1996)). In the first five of these six, groups of investigators used similar methodology (Schwartz, 1991, 1996; Dockery et al., 1992), applying a number of techniques to smooth out seasonal variability, and temperature/weather effects, though not a high-pass filter such as the 19-day weighted moving average. A problem associated with the use of a dummy variable as a seasonal filter, as in the Detroit MI (Schwartz 1991), St. Louis MO and Harriman TN (Dockery et al., 1992) studies, would be that the dummy variable would not act as a complete filter, being too coarse to allow detection of a weak ozone signal. Another problem of the Dockery et al. (1992) study, which was pointed out in the U.S. EPA Criteria Summary (1993), was the adjustment for the short-wave influences of temperature on mortality as a separate step prior to consideration of ozone. Since ozone is usually correlated with temperature, this would tend to pre-filter out the signal of interest, and might (improperly) remove all short-wave ozone-mortality association that is correlated with temperature. In addition, monitoring was conducted poorly in this study, and the single monitor in each large area might lead to considerable error in estimating population exposures, thus leading to misclassification.

Saldiva et al. (1995) performed a statistical analysis that included only 3 dummy variables for temperature and a monthly correction for season. This might not be adequate to demonstrate an association of mortality with ozone due to its high correlation with temperature and season. In Sao Paulo, ozone levels (38 ppb 1-h maximum) were low for a large Latin American city, while PM_{10} levels were very high (82 $\mu g/m^3$ annual mean), such that any weak effect of ozone could have been overwhelmed by the much stronger association of PM_{10}.

In the study by Dab et al. (1996) in Paris France, only respiratory mortality was examined, which had very low rate (9 deaths/day) compared with total mortality (37 deaths/day). This was probably insufficient to detect a significant association with ozone, although associations with mortality were found for PM_{13} and SO_2. In this study, temperature was treated as a linear variable although it is not the case, which could result in an underestimate of the ozone effects. In addition, the Paris analysis was carried out using only one of three ozone-monitoring networks, the one that was not representative of areas of high population density. This would result in more serious misclassification for ozone than for particulate matter, since large differences in ozone have been found between central-city and suburban monitors, while particulate matter concentrations usually are highly correlated across the region.

In the study by Zmirou et al. (1996) for Lyon France, only one monitoring site, in the urban centre, was available for ozone. This would increase the potential for scavenging of ozone by NO_2, and may not reflect actual population exposure to ozone. Ozone concentrations were much lower in this study (mean of 1-h maximum 7.75 ppb) than in any other locations listed in Table 12.1b. The relative risk of death (given originally for 50 $\mu g/m^3$ increases in pollutants or approximately 25 ppb for ozone) was 1.6% (95% CI: -2.4% to 6.4%) for a 10 ppb increase in ozone (1-h max). In this study, the only pollutant that showed a clear association with mortality was SO_2, although PM_{10} was associated with cardiovascular and respiratory mortality (to a lesser degree than SO_2). Interestingly, the authors used digestive mortality data as a control, since no prior association reported between air pollutants and digestive mortality. As expected, none of the pollutants showed any association with digestive mortality.

Wietlisbach et al. (1996) investigated the association between ozone and mortality in years 1984 to 1989 in Zurich and Basle, Switzerland. Semi-nonparametric Poisson regression models were used that included the pollution variables, a LOESS smooth of time to account for trend and seasonality, and a LOESS smooth of daily minimum temperatures. The authors reported a weak and inconsistent association between ozone and mortality in a single pollutant model. A significant association was found only in elderly population (>65 years) in Basle, but not in Zurich, and not in other age groups. When respiratory and cardiovascular mortalities were examined separately, ozone was not found to be associated with either of these, probably because of the low mortality rates. No adjustment for potential confounders was reported. The authors did not specify which ozone data (1-h maximum verse 24-h average) were used. Results were expressed as regression coefficients, but no standard deviation, or confidence interval or t values were reported.

Table 12.1b Summary of relative risk estimates in daily mortality for each 10 ppb increase in ozone, in univariate and multi-variate models

Location and reference	Ozone mean, ppb (range)(1-h max., unless indicated)	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion or exclusion in meta-analysis (S: Significant NS: Non-significant)
Detroit, MI (Schwartz 1991)	not given	no increase	----	**Results NS** Excluded, no quantitative results.
Los Angeles Co. CA (Kinney, Ozkaynak 1991)	75 ± 45	Increased, % not given	4%, O_3 and NO_2	**Results S** Excluded, no quantitative results for multi-variate model
St. Louis MO Harriman TN (Dockery et al. 1992)	22.5 ± 18.5 (24-h mean) 23.0 ± 11.4 (24-h mean)	24-h ozone: St. Louis: 0.29% (-1.18% to 2.94%),. Harriman: -0.64% (-3.93% to 3.29%)	---	**Results NS** Excluded, no quantitative results for multi-variate model
New York City NY (Kinney, Ozkaynak 1992)	56 (range not given)	[5.5 deaths per 10 ppb]	10%, O_3 and COH	**Results S** Excluded, no quantitative results for multi-variate model
Philadelphia PA (Li & Roth 1995)	19.8 ± 14.4 (24-h mean)	Increased for age 65y+ not increased for age <65	---	**Results S** Excluded, no quantitative results for multi-variate model
Philadelphia PA (Moolkavgar et al. 1995)	19.9 (year) (24-h mean) 35.5 (summer) (1.3-159)	Yearly data not given separately Summer: 1.5% (0.9-2.1%), 24-h ozone	Yearly: 0.62% (0.18- 1.04%) Summer: 1.5% (0.7-2.4%) +TSP, SO_2 24-h ozone	**Results S** Included
Los Angeles CA (Kinney et al 1995)	70 ± 41 (3-201), yearly	0.2% (0% - 0.5%), yearly ozone	0% (-0.44 to 0.4%) +PM	**Results S** Included
Toronto ON (Ozkaynak et al. 1995)	36 (95th centile 66)	(not given separately)	0.34% to 0.42% (+TSP)	**Results S** Excluded, an abstract
Sao Paulo Brazil (Saldiva et al. 1995)	38.3 + 29.7 (1-h max.), 12.5 + 11.5 (24-h mean)	For age 65+ years. 1-h: 0.4% (-0.42% to 1.03%); 24-h: -1.31% (-4.15% to 1.75%)	---	**Results NS** Excluded, no data
Philadelphia PA (Dockery et al. 1996)	not given	(not given separately)	0.9% (+$PM_{2.5}$)	**Results NS** Excluded, an abstract

Table 12.1b Summary of relative risk estimates in daily mortality for each 10 ppb increase in ozone, in univariate and multi-variate models

Location and reference	Ozone mean, ppb (range)(1-h max., unless indicated)	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion or exclusion in meta-analysis (S: Significant NS: Non-significant)
Chicago IL (Ito & Thurston 1996)	38 ± 19.9, yearly, 2-d average.	1.0% (0.6-1.5%), yearly ozone, 2-d average	2-day average ozone. 0.68% (0.08-1.16%) (+PM_{10})	**Results S** Included
Santiago Chile (Ostro et al. 1996)	52.8 (11-254)	Yearly: OLS model: -0.57% (-0.75 to –0.38%); Poisson: 0% (-0.19% to 0.38%) Summer: OLS model: 0.20% (0-0.50%) Poisson: 0.4% (0-1.0%)	Yearly: OLS model: -0.56% (-0.92 to 0%); Poisson: -0.20% (-0.56 to 0.20) Summer: OLS model: 0.38% (-0.57 to 1.32%); Poisson: 0.4% (0-0.9%) +PM_{10}	**Results S** Included
Mexico City DF (Loomis et al. 1996)	154 (26-319) (1-h max) 62 (12-130) (24-h mean), yearly	Yearly, 1-h max. ozone: 0.24% (0.11-0.39%) Yearly, 24-h max. ozone: 0.58% (0.22-0.94%)	Yearly, 1-h max. ozone: -0.18% (-0.52 to 0.16%) (+TSP and SO_2)	**Results S** Included
London UK (Anderson et al. 1996)	Yearly: 20.6 ± 13.2 (1-h max.), 15.5 ± 10.9 (8-h mean); summer: 7-36 (8-h) 11-45 (1-h)	Yearly ozone: 1-h max: 0.83% (0.42-1.25%) 8-h mean: 1.01% (0.46-1.57%); Summer: 1-h max: 1.03%(0.53-1.53%) 8-h mean: 1.2%(0.6-1.8%)	Yearly, 8-h average ozone: 1.14% (0.59 –1.69%) with black smoke. Summer, 8-h average ozone: 1.45% (0.7-2.19%) with BS. No 1-h max. data reported	**Results S** Included
Barcelona Spain (Sunyer et al. 1996)	28 (3.6-96) winter 44 (4.8-144) summer	Yearly: 0.96% (0.24-1.72%) Summer: 1.16% (0.34-2.02%)	---	**Results S** Excluded, no quantitative results for multi-variate model
Amsterdam NL (Verhoeff et al. 1996)	21.9 (4-41; 10-90th %), yearly	yearly ozone 0.98% (0.02-2.0%).	Yearly: 0.58% (-0.67 to1.9%) + BS 1.0% (-1.1 to 3.3%) + PM_{10}	**Results S** Included
Lyon France (Zmirou et al. 1296)	7.75 (0-72) (1-h max) 5.1 (0-40.2) (8-h mean), yearly	Increase not significant 1-h max.: 1.6% (-2.4% to 6.4%) 24-h avg.: 1.2% (-2.0% to 4.8%), yearly ozone	--- ---	**Results NS** Excluded, no quantitative results for multi-variate model
Paris France (Dab et al. 1996)	22.3 (3.1-74.8) (1-h max 14.1 (10-56) (8-h mean), yearly	Respiratory mortality only; Yearly ozone; 1-h max.: 0.8% (-1.3% to3.1%) 24-h avg.: 1.5% (-1.2% to 4.6%).	--- ---	**Results NS** Excluded, no quantitative results for multi-variate model

Table 12.1b Summary of relative risk estimates in daily mortality for each 10 ppb increase in ozone, in univariate and multi-variate models

Location and reference	Ozone mean, ppb (range)(1-h max., unless indicated)	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion or exclusion in meta-analysis (S: Significant NS: Non-significant)
4 APHEA cities: Athens Barcelona London Paris 3 additional cities: Amsterdam Basel Zurich (Touloumi et al. 1997)	47.7 ± 21.8 (all 1-h max) 36.8 ± 17.8 21.0 ± 13.2 23.5 ± 16.7 21.9 (4-41; 10-90th %) no 1-h values given for Basle or Zurich (8-h means 12 (B) and 14 (Z)), yearly ozone	Meta-analysis pooled estimate (random effects): For a single day: 1.16% (0.40-1.96%); Average of 2-5 day cumulative ozone: 0.96% (0.48 - 1.48%) Plus 4 non-APHEA cities: 1.16% (0.40% to 1.96%) (1-h max.) All yearly ozone data, 1-h max. ozone	Meta-analysis (random effects): 1.12% (0.20-2.00%) +BS 1.28% (-0.12% to 2.72%) +NO_2 Pooled estimates with non-APHEA cities not included in bivariate analysis	**Results S** Included for 4 APHEA cities.
Philadelphia PA (Kelsall et al. 1997, Samet et al., 1997)	19.9 ± 14.6 (2-day average) 8.3-28.5 IQR (=20.2)	2-d average ozone: 1.13% (0.4% - 1.9%)	2-d average ozone: 1.01% (0.02-2.0%)+TSP 1.11% (0.38-1.84%)+SO_2 1.12% (0.73-1.84%)+NO_2 1.17% (0.40-1.94%)+CO_2 0.96% (0.33-1.59%) + all four	**Results S** Included
Zurich, Basle and Geneva, Switzerland, 1984 – 1989. (Wietlisbach et al., 1996)	Mean ± SD (presumably 24-h average): Zurich: 13.4 ± 10.5; Basle: 12.0 ± 9.7; Geneva: 0	Data are expressed as regression coefficients; no SD or confidence interval reported. No ozone data for Geneva. For total mortality, no association in Zurich or Basle. For mortality of people >65 years of age, no association in Zurich, significant association in Basle (p<0.05). For respiratory and cardiac mortalities, no association in any cities.	---	**Results NS** Excluded, no relative risk data reported; exposure data not detailed (1-h max. vs. 24-h average).
11 Canadian cities (Burnett et al. 1998)	16.2 (24-h mean of 11 cities) IQR 13.3-35 (5-95th centile), yearly ozone	24-h ozone: 0.86% (0.35-1.37%), yearly ozone	24-h average ozone: 1.11% (0.66-1.56%) (+NO_2, SO_2, CO) (particles contribute another 1%)	**Results S** Included
13 Canadian cities [Burnett 1998 (special analysis for WGAQOG)]	31 (1-h max) (25-38 range of means, 13 cities) 32.9 ± 16.7 (16 cities)	0.79% (0.59-0.99%), yearly ozone	---	**Results S** Excluded, no data on multi-variate analysis; not in a peer reviewed journal

Ozone-only analyses, mean increase (%) in mortality ± SD = 0.613% ± 0.467% (n=17), per 10 ppb increase in ozone (1-h max.), 95% CI: -0.302% to 1.53%, p>0.05.

Table 12.1b Summary of relative risk estimates in daily mortality for each 10 ppb increase in ozone, in univariate and multi-variate models

Location and reference	Ozone mean, ppb (range)(1-h max., unless indicated)	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion or exclusion in meta-analysis (S: Significant NS: Non-significant)
Multi-pollutant analyses, mean increase (%) in mortality ± SD = 0.523% ± 0.444% (n=10), per 10 ppb increase in ozone (1-h max.), 95% CI: -0.347% to 1.39%, $p>0.05$.				
Meta-analysis of multi-pollutant analyses, weighted mean increase (%) in mortality ± SD = 0.399% ± 0.105% (n=10), per 10 ppb increase in ozone (1-h max.), 95% CI: 0.193-0.604%, $p<0.05$				

12.2.3 Effects of co-pollutants (Multi-pollutant studies)

Air pollution is always composed of a mixture of pollutants, often co-varying, and it is frequently difficult or impossible to separate the effects of one agent from the others. The statistical methods in time-series analysis make an assumption of independent action of the various pollutants in the atmosphere, which may not be the case. The net result with respect to association between pollutants and health endpoints may be due to a combination of ozone and PM, or ozone and one or more of the other pollutants that frequently co-occur with ozone.

Fourteen studies reported results using multi-variate models [Philadelphia (Moolkavgar et al. 1995, Kelsall et al., 1997, Samet et al. 997, Dockery et al. 1996), Chicago IL (Ito & Thurson 1996), Los Angeles (Kinney and Ozkaynak, 1991, Kinney et al., 1995), New York City (Kinney and Ozkaynak , 1992), Mexico City (Loomis et al., 1996),Toronto (Ozkaynak et al. 1995), 11 Canadian cities considered together (Burnett et al. 1998), London UK (Anderson et al. 1996), Amsterdam (Verhoeff et al., 1996), and a meta-analysis of 4 European cities (Touloumi et al. 1997)]. Eleven of these studies demonstrate a statistically significant positive association between ozone and mortality, with seven of them providing quantitative data. After adjusting for the effects of other pollutants, the relative risk (RR) for an increase in all-cause mortality varied between 0.27% and 1.12% per 10 ppb increase in ozone, measured as the 1-hour maximum. The mean RR (from studies with significant results, n=7) was an increase in daily mortality of 0.70% (standard deviation 0.35%) per 10 ppb increase in ozone, which is similar to single pollutant data [mean mortality increase is 0.65% per 10 ppb ozone (±0.36%), range 0.24% - 1.16%]. In almost all the cases with significant results, with particulate matter or SO_2 or NO_2 in bivariate analyses, ozone appeared to act independently from other air pollutants in the association of air pollution with increased mortality. Results for the individual co-pollutants are discussed in more detail below.

Three of these studies using multi-variate models reported a loss of the significance in the association between ozone and mortality when other pollutants were adjusted (Kinney et al. 1995, Verhoeff et al 1996, and Loomis et al. 1996). These three studies had reported positive associations between ozone and mortality in single pollutant analyses.

In the Verhoeff et al. (1996) study in Amsterdam, the Netherlands, the positive association between ozone and mortality was attenuated about 40% when particles as BS were included in a bivariate analysis. The RR for ozone declined from 1.05 to 1.03 (95% CI 0.97 to 1.10 for a 100 $\mu g/m^3$ or 50 ppb increase) while the RR for BS (100 $\mu g/m^3$) declined only 5% from a RR of 1.187 to RR of 1.178. The confidence limits for BS broadened considerably while the RR remained slightly above 1.0. With PM_{10} as the particle metric, the RR for ozone retained its magnitude while the RR for PM_{10} was reduced by 82%, from 1.187 to 1.034, and the confidence intervals for both pollutants included the null value (RR=1.0). When taking a closer look at the correlation analysis data, ozone was very weakly correlated with BS (r=-0.15) and PM_{10} (r=0.06), implying that ozone might have an independent relationship to mortality.

The statistical analysis in the Kinney et al. (1995) study for Los Angeles was thorough. However, the authors stated that the database on ozone was too small (every sixth day for six years or 364 days), and thus severely limited the power of the study to be able to discern an ozone effect when it was included with PM_{10} in a bivariate regression. Moreover the correlation coefficients between PM_{10} and ozone were high in this location (r=0.5) making it impossible to separate out their effects on mortality in this reduced data set.

The study by Loomis et al. (1996) in Mexico City ran into similar problems. As pointed out by the authors of this study, the associations found in ozone-only models were based on 715 days of monitoring, while the TSP plus ozone bivariate regressions were based on only 129 days of simultaneous monitoring, too few to provide consistent results. (Even 715 days provides a fairly small number of data points for a time-series analysis). In this particular case, total non-accidental mortality showed a much stronger association with 24-h average ozone concentration (RR=1.058, 95%CI 1.022-1.094%) than with current day 1-h maximal ozone concentration (RR=1.024; 95% CI 1.011-1.034 for 100 ppb increase) in models including temperature or seasonal adjustments. Moving average ozone and 10-h average ozone also had stronger associations with total mortality (RR= 1.043, 95% CI 1.021-1.064; RR=1.040, 95% CI 1.018-1.062, respectively) than 1-h maximum ozone. However, all bivariate or multi-pollutant analyses were undertaken using 1-h maximum ozone lagged 0 day, rather than any other measurement times (24-h, daytime maximum, and moving average, and a 1-day lag time). Had other ozone markers been used instead of the current-day 1-h maximum in multi-variate analyses, the associations might have been strengthened. Therefore this study provides inconclusive results regarding the attenuation of the ozone effect by TSP, or the independent effects of the two pollutants.

Although SO_2 had been associated with mortality in many of the early pollution episodes such as the London Fogs, bivariate regressions with ozone were performed only in a few studies. In the Moolkavgar et al. (1995) report on Philadelphia, SO_2 was associated with mortality in both an all-year and a summer-only analysis. When both summertime ozone and summer SO_2 were regressed together, both retained their positive associations equally, but inclusion of TSP as a third variable resulted in the decline of the regression coefficient for SO_2 and TSP, with retention of the association for ozone. Later analyses of the Philadelphia data (Kelsall et al. 1997, Samet et al., 1997) qualitatively agreed with the previous findings. In these studies, the relative risks for ozone were reduced but still significant and the relative risks for SO_2 increased from 1.011 to 1.023. In Mexico City (Loomis et al., 1996), the significant association of mortality with ozone from single-pollutant analysis was no longer seen when ozone was included in a three-pollutant regression with SO_2 and TSP (the results of a bivariate regression with SO_2 were not given). In London UK, both ozone and SO_2 were positively associated with premature mortality in single-pollutant analyses, and the text stated that both retained their associations when regressed in bivariate regressions, but no values were provided (Anderson et al., 1996). In an analysis conducted in 11 Canadian cities, Burnett et al. (1998) reported that a 5.4 ppb increase in 24-hour mean SO_2 (average of 11 cities) contributed a 1.4% increase (95% CI 1.1% to 6.2%) to premature deaths, when all other pollutants including ozone were included in a multivariate regression. This was approximately one-sixth of the estimated 8.2% of all non-accidental deaths ascribed to air pollution. In the same analysis, a 16.2 ppb rise in 24-h ozone (average of 11 cities) contributed 1.8%, or about one-quarter of the total 8.2% ascribed to air pollution. The average correlation between ozone and SO_2 was low (-0.2) and varied between -0.3 and 0.0 in the 11 cities individually. Overall, based on the evidence from all the available studies, it appears that the associations of both ozone and SO_2 with premature mortality are independent of each other in locations where both are associated with mortality in single regressions.

Regressions including both ozone and NO_2 have been conducted in five studies, in Los Angeles (Kinney & Ozkaynak, 1991), Philadelphia PA (Kelsall et al., 1997, Samet et al., 1997), London UK (Anderson et al., 1996), a meta-analysis on 4 European cities (Touloumi et al., 1997), and a study on 11 Canadian cities (Burnett et al., 1998). Kinney & Ozkaynak (1991) reported that ozone and NO_2 together accounted for 4% of all deaths in Los Angeles. In Philadelphia, ozone was strongly and independently associated with premature mortality in bivariate regression, while NO_2 was not. The ozone coefficient was virtually unchanged in bivariate regressions, while NO_2 did not associate with mortality in either single-variate or bivariate models (Kelsall et al., 1997; Samet et al., 1997). When ozone was included in a multi-variate regression with all five of the air pollutants including NO_2, its coefficient was only slightly reduced, and for a 10 ppb increase in ozone, mortality increased 0.96% (95% CI: 0.3-1.6%). In a meta-analysis (Touloumi et al. 1997) which included four European cities, both ozone and NO_2 were independently associated in bivariate regressions. The relative risk for ozone declined only slightly from 1.029 to 1.025, and the RR for NO_2 rose slightly from 1.013 to 1.015. In the 11-Canadian city study, Burnett et al. (1998) reported that a 23.5 ppb increase in 24-hour mean NO_2 (average of 11 cities) contributed a 4.1% increase (95% CI 1.1% to 6.2%) to premature deaths. This was observed when all other pollutants including ozone were included in a multi-variate regression analysis. This was approximately 50% of the estimated 8.2% of all non-accidental deaths ascribed to the gaseous component of air pollution. The average correlation between ozone and NO_2 was low (-0.1) but varied between -0.5 and 0.2 in the 11 cities individually. The evidence from these five studies supports the independent associations of both ozone and NO_2 with premature mortality when the two are examined together.

Only limited numbers of studies (Kelsall et al., 1997, Samet et al. 1997, Burnett et al. 1998) have examined the relationship of ozone to mortality in multi-pollutant analyses with more than two air pollutants normally considered, i.e. PM, SO_2, NO_2, and CO. In the Philadelphia analysis by Samet et al. (1997, also in Kelsall et al., 1997), the ozone coefficient remained stable and significant when regressed together with TSP, SO_2, NO_2 and CO. In this study, the correlation coefficients between ozone and other pollutants were moderate (r for TSP, SO_2, NO_2 and CO were 0.12, -0.02, 0.001 and –0.2, respectively), indicating that ozone acts independently on mortality. In the study by Burnett et al. (1998), the ozone coefficient also remained a significant predictor of mortality when regressed together with NO_2, SO_2, CO, and particles (stated in text but data not shown). In this study the correlation coefficients between ozone and other pollutants were generally moderate (below 0.2 to 0.3), but correlation coefficients in individual cites and between other pollutants were as high as 0.6. Some caution is therefore warranted in the attempt to establish the role of ozone or of the other pollutants in prediction of premature mortality from the results of this study.

Overall, a majority of studies that conducted bivariate and multi-variate analyses have confirmed the association between ozone and premature mortality that was seen in the single-pollutant analyses. The independence of this assocation from associations with particles, SO_2 and NO_2 was established in various locations with different pollutant mixes, thus giving external consistency to the results.

12.2.4 Summary of mortality data and meta-analysis

On balance, the time-series studies reviewed here, most of which received extensive statistical treatments, indicate that the association between ozone and mortality is positive, consistent, and independent of other co-occurring air pollutants including particulate matter. Seventeen of the 23 studies reviewed reported statistically significant positive associations using single pollutant models. Fourteen studies reported results using multi-pollutant models, eleven of which demonstrated statistically significant independent associations between ozone and mortality. These associations were found in cities across North America, in four U.S. and 13 Canadian locations, in Santiago Chile and three European cities, and in a meta-analysis including seven European cities, demonstrating consistency of results despite widely varying climatic conditions, pollutant mixtures, population compositions, and life styles.

These associations were reported for cities with mean ozone concentrations (expressed as the one-hour maximum) between 20 and 75 ppb, i.e. below, and in most cases well below the current Canadian Air Quality Objective for ozone of 82 ppb.

For meta-analysis, there are two basic models by which variances are used to weight the estimates from different studies in a pooled estimate. One is the fixed effects model, which assumes that there is a single true concentration-response relationship, and therefore a single true value for the relative risk. The second model is the random effects model, which assumes that the relative risk from different studies may in fact be estimates of different risks, rather than just different estimates of a single underlying parameter. The reason for this assumption is that the behavior or susceptibility of populations varies among study locations, resulting in a potential difference in the relationship between health effects and ambient ozone concentrations. In this document, ten mortality studies that met the criteria in Section 12.1.4 were included (Table 12.1b) in a meta-analysis, and the random effects model was assumed when the null hypothesis of a single underlying relative risk parameter {expressed as [(RR-1) x 100]} was rejected using a test statistic, Q_w.

A pooling of ten studies with adjustments for seasonal cycles and weather terms, and with a simultaneous inclusion of co-pollutants, reveals that the weighted relative risk of total non-accidental mortality is 1.040 (95% CI 1.019 – 1.060) for 100 ppb 1-h maximum ozone [or 0.40% increase in mortality (95% CI 0.19 – 0.60%) per 10 ppb increase in ozone]. This value is in line with the relative risks from other meta-analyses reported by Thurston and Ito (1999)(RR=1.036 per 100 ppb increase in 1-h maximum ozone, 95% CI 1.023-1.050), and by the US EPA (1997)(RR=1.029 per 100 ppb increase in 1-h maximum ozone).

Using the data from 13 Canadian cities (Burnett, 1998, in Appendix A) to conduct single-pollutant regression analyses, the results show that the risk for non-accidental mortality is 0.79% per 10 ppb increase in daily one-hour maximum ozone (95% CI: 0.59-0.99%). The Lowest observed adverse effect level (LOAEL) with statistical significance is 20 ppb ($p<0.001$). The data continue to show a trend of positive association with ozone values as low as 10 ppb. There appears to be no threshold for mortality.

Six studies did not find any association between ozone and mortality. Although similar methodology was used for each of these studies, some differences in the statistical treatment and/or shortfalls (e.g. small ozone sample size, or data from only one monitor, or respiratory mortality data only) were identified. These differences might explain the lack of association between ozone and mortality for some of the studies.

Although less information was available on the concentration-response characteristics for mortality than for hospitalization data, several studies indicate that the relationship is more or less in a linear pattern, down to less than 10 ppb without evidence of any threshold or flattening out of the response curve at low concentrations. Only a few studies provided evidence of a more specific cause of death; cardiovascular deaths were associated with ozone increases in several studies while respiratory deaths were not, possibly because of proportionally fewer deaths in this category.

12.3 MORBIDITY STUDIES—ACUTE EFFECTS: HOSPITALIZATIONS

The short term effects of ambient air pollutants on morbidity have been investigated in a number of studies, using administrative data on hospital admissions or emergency room visits. These are advantageous in providing an objective measure of adverse effects, particularly in Canada where the cost of medical care is not a deterrent to seeking hospitalization, due to universal free medical coverage. Despite the fact that hospitalizations represent only the serious outcomes, and are the tip of the iceberg with respect to the number of people adversely affected by a pollutant, hospitalizations as an endpoint have proven to be surprisingly sensitive indicators of adverse health outcomes. This is due to the extremely large size of some of the populations studied and to the advanced statistical methods employed. This has allowed for detection of small effects in susceptible subpopulations that would not be detected in clinical studies, partly because of ethical considerations. Table 12.2a contains detailed information on hospital admission studies. The data are summarized in Table 12.2b to assist in understanding the information.

Table 12.2a Ambient ozone and association with hospitalizations

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Burnett et al., 1994 Southern Ontario (pop. 8,700,000) 1983-1988 (6 years; 2191 days) 168 hospitals	Respiratory admissions: -Asthma (39%) -COPD (25%) -Infection (36%) All ages categorized into group: <2y (12%), 2-34y (30%), 35-64y (22%), 65 +y (36%) 235,532 respiratory visits; 107/d	O_3 1-h max: 52 ppb (May-Aug) 95th percentile was 92 ppb (range 62-118 ppb) <40 ppb (other months) 22 monitoring sites (correl high: r=0.68)	Daily mean of some pollutants were measured (data not given): SO_2 (24 sites) NO_2 (18 sites) SO_4 (9sites) daily mean: 5.34 ?g/m^3 Also monitored temperature, relative humidity and pressure	-Multiple regression analysis, using weighted 19-weighted linear filter for removal of seasonal cyclic variations -Dummy variables for day-of-week effects and for inter-hospital differences -Same day and lag days 1,2 and 3 were checked	-There is a highly significant relationship (p<0.001) between 1-h peak O_3 concentrations recorded previous day an respiratory admissions during the summer months of May-August -Respiratory admissions for all ages were significantly increased by air pollution (ozone + sulphates): Asthma= 7%, COPD= 6% and Infection=4%, all diseases=5.8%. -Increase of 5% of admissions was associated with a increase in ozone from 0 to 50 ppb. -Association with sulphates (lagged 1 day) was also positive for hospital admissions (RR= 1.003-1.035 for a 5 ?g/m^3 increase in sulphates). -Asthma was the most significantly affected in children (<14y), an 8.2% increase in asthma admission per 50 ppb increase (p=0.005) -No correlation for negative control -Neither SO_2 or NO_2 are considered to be a strong confounder for ozone or sulphates
Burnett et al., 1997a 16 cities across Canada (pop. 12,600,000) April 1981 to December 1991 (10 years; 3927 days) 134 hospital	Respiratory admissions (not broken down into subcategories) Mean admissions: 720,519 respiratory visits; 183/d	O_3 1-h max: Spring: 40 ppb Summer: 38 ppb Fall: 21 ppb Winter: 26 ppb Whole year: 31 ppb (95th percentile 60 ppb)	Average on available data on an hourby hour basis: SO_2: 14.4 ppb NO_2: 35.5 ppb CO: 2.2 ppm CoH: 0.64 (1000 in ft) Dew point and temperature (daily maximum and minimum) also recorded	- Multiple regression analysis using a 19-weighted linear filter to detrend seasonal cyclic variations -Dummy variables for hospitals effects, day to day variations, location and weather -Looked at different lag times, considered admissions same day and lag 1, 2 day	-1-h max, 30 ppb incr. Of ozone (single variate): Winter: 0.994 (95% CI 0.964-1.025); Spring: 1.042 (1.012-1.073); Summer: 1.05 (1.026-1.074); Fall: 1.028 (0.998-1.059). -Single-variate model, the ozone risk for hospital admissions (for respiratory diseases) for 16 cities, April-Dec. is: 1.042%/30 ppb increase in daily 1-h maximum ozone (t=5.12, p<0.05). -Multi-variate models, RR (t ratio): 1.043 (4.45), +CO 1.031 (3.04), +CO, dew point temperature 1.024 (p=0.0258), +CO, dew point temperature, PM (soiling index), in 11 cities with available PM data. -O_3 levels measured on the day previous to admission were more strongly related to respiratory hospitalizations. Associations were also observed on the same day and lags 2 days -No association for control negative. -The RR (30 ppb increase) for elderly (>65 y, RR=1.040, 95%CI 1.01-1.072) was similar to that for younger patients aged <65 y (RR=1.045, 95%CI 1.021-1.068)

Table 12.2a Ambient ozone and association with hospitalizations

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Burnett et al., 1997b Toronto, Ont. 1992-1994	Total respiratory admissions (ICD-9 464-466, 490, 480-486, 491-494, 496) Cardiac admissions (ICD-9 410-414, 427, 428)	Daily 1-h max. 41.2 ppb (5th-95th percentile 22-69 ppb) When regression was done, used 3 day average levels.	PM_{10}: 28.4 µg/m^3 $PM_{2.5}$: 16.8 µg/m^3 Sulphate: 57.1 nmol/m^3 H^+: 5 nmol/m^3 NO_2:38.5 ppb SO_2:7.9 ppb CO: 1.8 ppm.	Logistic regression models were used for associations of hospitalizations with pollutants. Seasonal cycle and day of the week were controlled using nonparametric smoothed curve using LOESS. Multi-variate models were used to control co-pollutants. Temperature was co-regressed with pollutants.	-The study focused on PM effects. -Single pollutant models, not controlled for temperature and dew point temperature, at 11.5 ppb ozone (3-d avg.); lag 1 day: respiratory admissions: RR=1.068 (t ratio=6.19) cardiac admissions: RR=1.057 (3.52) -Single pollutant models, controlled for temperature and dew point temperature (11.5 ppb, 3-d avg.), lag 2 days: respiratory admissions: RR=1.064 (t ratio=5.13) cardiac admissions: RR=1.074 (3.85) -multi-variate analysis not done for ozone, but for PMs -Correlation of ozone was: with sulphate (r=0.53), PM_{10} (r=0.23), $PM_{2.5}$ (r=0.32) and H^+ (r=0.34).

Burnett et al., 1997c
10 Canadian cities (1981-1991)
	Congestive heart failure (ICD-9 427) in the elderly >65 y.	Daily 1-h max.: 32 ppb (5th –95th percentile: 10-64 ppb)
		24-h avg.: 16 ppb (5th-95th percentile 3-35 ppb)
			Coefficient of haze (CoH): 0.7 10^3 ln ft
			NO_2:39 ppb
			SO_2: 13.1 ppb
			CO: 2.32 ppm.
				Logistic regression models were used for associations of hospitalizations with pollutants.
				Seasonal cycle and day of the week were controlled.
				Multi-variate models were used to control co-pollutants.
				Temperature was co-regressed with pollutants.
					-The study focused on CO effects.
					For ozone effects (24-h average ozone) on congestive heart failure, lag 2 d, at 16 ppb ozone:
					-Single pollutant models, not controlled for temperature and dew point temperature: log-RR coefficient=0.0021 (t ratio=2.2);
					-Single pollutant models, controlled for temperature and dew point temperature:
					log-RR coefficient=00.0022 (t ratio=1.8);
					-multi-variate analysis, controlled for temperature, DP temperature, and all the pollutants:
					log-RR coefficient=0.0021 (t ratio=2.0);
					-City-specific RR was also calculated, but only for CO.
					-Correlation of ozone was negative with other pollutants (r=-0.36 to –0.15).

Table 12.2a Ambient ozone and association with hospitalizations

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Bates and Sizto, 1987;1989 Southern Ontario (smaller area than the Burnett et la. 1994 study) (pop. 5,900,000) 1974 and 1976-1983 (9 years) Winter (Jan.-Feb.) Summer (July-Aug.) 79 hospitals	All respiratory admissions All ages separated into groups: -0-14y -15-60y -61+y 1,282,064 visits in winter where 2.9% for respiratory visits 1,223,054 visits in summer where 1.8% for respiratory visits	O$_3$ 1-h peak: Winter: 23.34 ppb Summer: 56.07 ppb 17 monitoring stations	Monitored every hour: SO$_2$ CoH SO$_4^=$ winter: 9.51 µg/m^3 and summer: 10.31 µg/m^3 on a basis of 24-h period every 6th day Also monitored daily temperature and relative humidity 17 monitoring stations	-Multiple regression analysis -They compared the number of admissions on each day only with the average number of admissions for the same day of the week (Tuesday), in the same season, of the same year.	-Significant association ($p<0.001$) between respiratory admissions and 1-h peak O$_3$ in summer (lagged 1 or 2 days) -O$_3$ correlated with respiratory admissions minus asthma, but lagged 2 days only -O$_3$ correlated with total asthma admissions in all ages except with asthma in children aged 0-14y -SO$_4$ and SO$_2$ were correlated to the same three endpoints with about the same lad times for SO$_4$ and a lag of 2 days only for SO$_2$ -CoH was not correlated to any of the respiratory admissions - O$_3$, SO$_4$ and temperature together, all lagged 0,1,2 days: 5.6% of variability in respiratory admissions (temperature alone accounts for less than 1% of the variance and SO$_4$ accounts for about 3%)
Delfino et al., 1994. May-Oct. and Aug.-July, 1984-1988, Montreal (population about 3 million in 1986).	All age respiratory admissions (ICD-9); all age non-respiratory admissions; ages 0-18 non-respiratory admissions.	Ozone 1-h max.: May-Oct. 36 (90^{th}: 59.2); July and Aug.: 41 (90^{th}: 65.8). Ozone 8-h max.: May-Oct. 30.4 (90^{th}: 51.5); July and Aug.: 35 (90^{th}: 57.3)	PM$_{10}$ 24-h mean: May-Oct. 29.5 (90^{th} 45.7) µg/m^3 July and Aug. 31.5 (90^{th} 48) µg/m^3 SO$_4$: 24-h mean: May – Oct: 4.2 (90^{th} 8.2) µg/m^3 July and Aug. 4.9 (90^{th} 9.7) µg/m^3	-A High-pass filter (19-d moving average) used to eliminate yearly seasonal trends in the data; -day-of week trends controlled by prefiltering the outcome variables prior to analysis; -Ordinary least-squares used to regress single air pollutants on the outcome; -Coregressions of ozone with PM	-Respiratory admission regression coefficient (t ratio) for 8-h average ozone was 0.025 (2.6) per µg/m^3 ozone increase, 0.676%±0.26% increase in respiratory admissions per 10 ppb ozone. -Ozone and temperature were both non-significant when entered into regression model simultaneously. Regression coefficient for ozone (8-h average) was 0.015 (t ratio 1.22) when temperature was regressed simultaneously, 0.405%± 0.332% increase in respiratory admission per 10 ppb ozone. -Asthma admissions when ozone was co-regressed with PM$_{10}$, regression coefficient for ozone (1-h max.) was 0.004 (t ratio 0.89), 0.175%±0.197% increase in asthma admissions per 10 ppb ozone. -Respiratory non-asthma admission when ozone was co-regressed with sulphate, coefficient for ozone (1-h max.) was 0.04 (t ratio 0.07), 1.65%±23.61% increase in non-asthma respiratory admissions per 10 ppb ozone.

Table 12.2a Ambient ozone and association with hospitalizations

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Thurston et al., 1994 a,b Toronto (pop. 2,400,000) July-Aug 1986-1988 (3 summers; 117 days) 22 hospitals	Total respiratory (mean 13.77 admissions/d) and asthma hospital admissions (mean 8.94 admissions/d)	O_3 1-h max: 49.3 ppb (1986) 53.4 ppb (1987) 69.7 ppb (1988) Mean 57.5 ppb (3 years) 2 days > 120 ppb 22 days > 80 ppb	Daily maximum 1-h: SO_2: 1.7 pphm NO_2: 4.73 pphm Daily 24-h average: SO_4: 7.5 $\mu g/m^3$ H^+: 28.77 nmole/m^3 PM_{10}: 32.9 $\mu g/m^3$ $PM_{2.5}$: 18.6 $\mu g/m^3$ TSP: 71.73 $\mu g/m^3$ Also monitored daily temperature Three sites	-Detrend for hospitalization, pollutant and temperature data, and controlling for day-of-the week effects -Bivariate correlation analysis -Same days and lagged/followed 1,2,3 were checked	-Only the O_3, H^+, and SO_4 associations with respiratory/asthma admissions remained significant after controlling for temperature. Admissions increased 3.83%±1.43% for 10 ppb ozone, 1.68% for 10 $\mu g/m^3$ H^+, 0.77% for 10 $\mu g/m^3$ sulphate, single-pollutant models + temperature. -In two pollutant models, ozone associations were still significant, and admissions increased 3.64%±1.48% per 10 ppb ozone (+ H^+), 3.68%± 1.5% (+sulphate), 2.93%±1.69% (+fine particles), 2.81%±1.75% (+PM10), and 2.61%±1.65% (+TSP). Only H+ (1.11% increase in admission per 10 $\mu g/m^3$) and sulphate (4.5% increases in admissions per 10 $\mu g/m^3$ remained significant when co-regressed with ozone. -O_3 was still strongly significant after excluding days with maximum 1-h O_3 > 120 ppb -Summertime haze air pollution was associated with 24% of all respiratory admissions (21% with O_3, 3% with H^+) -The slope for all 117 days was 0.051 admission/ppb ozone. It decreased to 0.048 when the 2 days > 120 ppb were removed, and to 0.045 when all days above 80 ppb were removed. -Temperature, NO_2 and SO_2 associations with respiratory/asthma admissions were weaker and less definitive -The highest correlations among the pollution variables, and between the pollution and temperature, almost occurred with zero lag -The authors concluded that there was no clear discrimination of a single pollutants as the responsible agent, but the regression suggest that O_3 was the summertime haze constituent of greatest relevance to hospital admissions

Table 12.2a Ambient ozone and association with hospitalizations

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Thurston et al., 1992 Albany (991,477); Buffalo (2, 047,669); White Plains (1,956,695) and New York City (7,322,564) June-Aug. 1988-1989 (2 summers; 92 days)	Total respiratory and asthma admissions Respiratory admissions: -Albany: 12.5/d -Buffalo: 24.35/d -NYC: 136.95/d -White Plains: 24.9/d Asthma admissions: -Albany:2.55/d -Buffalo: 6.85/d -NYC: 52.15/d -White Plains: 6.55/d	O_3 1-h max (ppb): 1988 -Albany: 64-148 -Buffalo: 75-164 -NYC: 69-206 -White Plains: 84-179 1989: -Albany: 55-112 -Buffalo: 65-128 -NYC: 53-111 -White Plains: 60-123	Also monitored: H^+ SO_4 Also monitored: daily temperature	-Daily counts of unscheduled (emergency) hospital admissions with a primary diagnosis of respiratory illness -Detrend for the summer admissions and environmental data, and also controlling for day-of-the week effects -Multiple regression analyses and cross-correlation analyses -Same day and lagged/followed 1,2 and 3 days were checked.	-Strong associations between elevated summer haze pollution (O_3, H^+, SO_4) and increased total respiratory and asthma admission on the same day and/or subsequent days in Buffalo and New York City, especially during the summer 1988. -For Buffalo and NYC, RR of total respiratory admissions is 1.22 ±0.12 (89 ppb) and 1.19±0.04 (137 ppb) respectively for ozone (based on the 1988 high-pollution summer, +temperature). - For Buffalo and NYC, RR of asthma admissions is 1.29 ±0.12 (89 ppb) and 1.23±0.10 (137 ppb) respectively for ozone (based on the 1988 high-pollution summer, +temperature). -Lag times were 0-3 days with lad 2 days most highly correlated with ozone -Pollution-admissions remained significant ($p<0.05$) even after the simultaneous inclusion of lagged daily maximum temperature.
Schwartz, 1994a Birmingham, Alabama (pop. 590,591) 1986-1989 (4 years)	Hospital admissions of elderly: -pneumonia (5.93/d range 5.08 to 7.85) -COPD (2.16/d range 1.82 to 2.55)	O_3 24-h avg.: Winter:- Spring: 28 ppb Summer: 28 ppb Fall: 18 ppb Mean: 25 ppb (10-90% 14-25 ppb)	PM_{10}: Winter: 40 µg/m^3 Spring: 47 µg/m^3 Summer: 49 µg/m^3 Fall: 44 µg/m^3 Also monitored weather variables: temperature and dew point	-Daily counts of pneumonia and COPD admissions -Poisson regression analysis (controlling for time trends, seasonal fluctuations and weather)	-No association with pneumonia admissions and ozone concentrations on the same day. -Weak association with pneumonia admissions and ozone 2 days before the admissions (RR= 1.14, 95% CI 0.94-1.38 for 50 ppb increase in ozone, 24-h avg.). The association was not due to the coincidence of high ozone with high-temperature days, since it persisted when they were excluded (days> 120 ppb)) -Weak association with COPD admissions and ozone 1-day lag (RR=1.17, 95% CI 0.86-1.60 for 50 ppb increase in ozone, 24-h avg.). -1-h max. ozone: pneumonia: 1.04 (95%CI 0.97-1.12) for 50 ppb; COPD: 1.07 (95%CI 0.96-1.20) -For an increase of 100 µg/m^3, inhalable particules were a risk factor for pneumonia admissions (RR=1.19, 95% CI 1.07-1.32) and for COPD admissions (RR=1.27, 95% CI 1.08-1.50) -Temperature correlated for both PM_{10} and ozone -Correlation between PM_{10} and ozone (correl. low: r=0.29) -Results not sensitive to methods of analysis or to extremes temperature

Table 12.2a Ambient ozone and association with hospitalizations

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Schwartz, 1994b Detroit, Michigan (pop. 4,382,000 were 517,000 are 65yr of age or older) 1986-1989 (4 years)	Hospital admissions, 65 yr of age or older -Pneumonia (15.7/d) -COPD (5.8/d) -Asthma (0.75/d)	O_3 mean 24-h average: 21 ppb (10-90% 7-36 ppb) O_3 mean peak (1-h max.): 53 ppb 1986-1989: 9 monitoring sites 1987-1988: 8 monitoring sites O_3 data were available for 85% of the days during the study period	PM_{10} collected over a 24-h period: mean 48 µg/m^3 Monitoring stations in operation for PM_{10}: 1986: 2; 1987: 6; 1988: 7; 1989: 4 PM_{10} data were available for 82% of the days during the study period Also monitored weather variables: daily temperature and dew point	-Daily counts of pneumonia (ICD-9, 480 to 486) and COPD (ICD-9, 490 to 496) admissions of persons aged 65 years or older -Poisson regression analysis -Dummy variables for each months (controlling for seasonal and other long-term temporal trends, temperature and dew point)	-Asthma admissions were not associated with either pollutants -Pneumonia: PM_{10} (RR=1.012, 95% CI 1.019-1.004) and 24-h ozone concentrations (RR=1.026, 95% CI 1.040-1.013) were associated with daily admissions for pneumonia. The relative risk is for 10 µg/m^3 increase in PM_{10} and 5 ppb increase in 24-h ozone concentrations, two-pollutant models. A similar but weaker effect was found for 1-h max. ozone. -COPD were associated with PM_{10} (RR=1.020, 95% CI 1.032-1.009) and ozone (RR=1.028, 95% CI 1.049-1.009). The relative risk is for 10 µg/m^3 increase in PM_{10} and 5 ppb increase in 24-h ozone concentrations, two-pollutant models. -Controlling for one pollutant did not effect the magnitude of the association with the other pollutant -Correlation between PM_{10} and O_3: r=0.35 -Correlation between O_3 and temperature: r=0.67 -Concentration-response relationship for pneumonia admissions for PM is linear, while for ozone it shows a potential threshold at 25 ppb. When PM exceeding 150 µg/m^3 and ozone exceeding 120 ppb were eliminated in the regression models, the associations remain significant, RR 1.012 (95%CI 1.019-1.004) for PM, and RR 1.026 (95%CI 1.040-1.013) for ozone; both for pneumonia, two-pollutant models. -Same treatment for COPD, when PM above 150 µg/m^3 and ozone above 120 ppb were eliminated in the regression models, the associations remain significant, RR 1.018 (95%CI 1.033-1.004) for PM, and RR 1.032 (95%CI 1.056-1.008) for ozone; both for pneumonia, two-pollutant models.

Table 12.2a Ambient ozone and association with hospitalizations

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Schwartz, 1994c Minneapolis-St. Paul, Minnesota (pop 2,460,000) 1986-1989 (4 years, 1461 days)	Hospital admissions, 65 years and older -Pneumonia (6/d) -COPD (2.2/d)	O_3 mean 24-h: 26 ppb 6 monitoring stations in 1986 and only four in 1987-1989 O_3 data were available for 99% of the days during the study period	PM_{10} collected over a 24-h period: 36 $\mu g/m^3$ PM_{10} data were available for 86% of the days during the study period 2 sites in 1986 through 88 and four sites in 1989 Also monitored weather variables: temperature and dew point	-Daily counts admissions, by admit rate, for pneumonia (ICD-9, 480-487) and COPD (ICD-9, 490-496) of persons aged 65 years or older -Poisson regression analysis with dummy variables for each 48 months and for 8 categories each of temperature and dew point. Linear and quadratic time terms were also included	-PM_{10} was a risk factor for pneumonia admissions. For single pollutant model, RR =1.17 (95% CI=1.33-1.03). For multi-pollutants model with ozone and temperature, RR=1.18 (95% CI=1.03-1.36), for 100 $\mu g/m^3$. -Ozone was also associated with pneumonia admissions. For single pollutant model, RR=1.19 (95% CI=1.02-1.40), 50 ppb, 24-h avg. For multi-pollutant with PM and temperature, pneumonia RR=1.22 (1.02-1.47) for 50 ppb, 24-h average. -When days exceeding 150 $\mu g/m^3$ PM10, and 120 ppb ozone were excluded, the association remained for pneumonia (RR=1.17, 95% CI=1.35-1.02 for PM_{10}, and RR=1.15, 95% CI=1.37-0.96 for ozone). -Association between PM10 and COPD was also significant. -Correlation between PM_{10} and O_3: r=0.18 -Correlation between O_3 and temperature: r=0.51
Schwartz, 1995 New Haven, Connecticut Tacoma, Washington 1988-1990 (3 years, 1096 days)	Respiratory admissions (ICD-9, 460-519) for 65 years of age or older New Haven: 8.1/d Tacoma: 4.2/d	O_3 April to October, 24-h avg. New Haven: 28.6 ppb (10-90%, 15.8-45.4 ppb) Tacoma: 24.5 ppb (10-90% 13.3-35.7 ppb)	Pollutant measured on a 24-h period New Haven: PM_{10}: 41 $\mu g/m^3$ SO_2: 78 $\mu g/m^3$ Tacoma: PM_{10}: 37 $\mu g/m^3$ SO_2: 44 $\mu g/m^3$ Also monitored weather variables: temperature and relative humidity	-Daily counts of respiratory admissions of person aged 65 years or older. -Multiple regression analysis using a 19-day weighted linear filter (as Burnett and co-workers)	-All three pollutants were associated with respiratory hospital admissions of the elderly -For total respiratory admissions, ozone in single pollutant model RR =1.06, 95% CI=0.99-1.13 in New Haven, and RR=1.21, 95% CI=1.06-1.38 in Tacoma, for a 50 $\mu g/m^3$ ozone (25.5 ppb). -In two-pollutant models, for a 25.5 ppb increase in ozone, in New Haven, RR=1.07, 95% CI=1.00-1.15 with PM, and RR=1.05 (0.98-1.13) with SO_2. in Tacoma, RR=1.20 (95% CI=1.06-1.37) with PM, and RR=1.21 (1.06-1.37) with SO_2

Table 12.2a Ambient ozone and association with hospitalizations

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Schwartz, 1996 Spokane, WA. Jan. 1988 – Dec. 1990	Respiratory admissions of patients 65 years or older, (ICD-9 460-519) (ICD-9 480-487, pneumonia, and ICD-9 490-496, COPD, were the largest subcategories). Total 4241 respiratory hospitalizations, 1137 for COPD; 267 for asthma, 2049 for pneumonia. Elderly (≥65 y)	1-h max. (converted from μg/m^3): 40.3 ppb (10-90% 29.6-55.6 ppb); 24-h average (converted from μg/m^3): 28.6 ppb (10-90% 20.4-37.2 ppb).	PM_{10} Daily average: 37 (10th to 90th: 16-83) μg/m^3	-Generalized additive model to remove long wavelength correlations between air pollution and morbidity. -Linear Poisson regression for daily number of admissions on smooth functions of day of study, temperature, dew point temperature, and day of week indicators.	-Correlation of ozone with temperature was 0.436, with PM10 was 0.259, regarded as low. -Per 25.5 ppb increase of ozone (1-h max. or 24-h average), for all respiratory admissions (single pollutant models): 1-h max.: RR 1.244 (95%CI: 1.002-1.544); 24-h avg: RR 1.284 (95%CI: 0.926-1.778). -For pneumonia: 1-h max. RR: 1.279 (95%CI: 0.947-1.727) -for COPD: 1-h max. RR: 1.125 (0.764-1.656). -Without extreme temperature days (excluding 2.5% of days of coldest weather and 2.5% of days of hottest weather): 1-h max. RR: 1.133 (0.901-1.442). -Including a 2-demensitoal smooth vs temperature and humidity: 1-h max. 1.241 (1.001-1.538). -Including smooth functions of temperature on the same day and 4 preceding days: 1-h max. RR: 1.38 (1.09-1.749).
Moolgavkar et al., 1997 Minneapolis-St. Pau, MN Birmingham, AL Jan. 1986-Dec. 1991	Total respiratory Pneumonia COPD Elderly (≥65 y)	24-h ozone: mean (10th to 90th percentile): Minn: 26.2 ppb (13.5-40.1 ppb), data avaliable for all seasons Birm: 25.1 (13.5-37.6 ppb), data not available in winter.	PM10 (μg/m^3): Minn:33.98; Birm: 43.44 SO2 (ppb): Minn: 4.82; Birm: 6.58 NO2 (ppb): Minn: 16.3; Birm: no data CO (ppm): Minn: 1.6; Birm: 1.23	Semiparametric Poisson regression models were used for analyses of the data. Temperature and day of study (to adjust for temporal trends and variations in hospital admissions not attributable to pollution or weather) were adjusted by nonparametric smoothers. PM_{10}, NO_2, SO_2 and CO were concurrently adjusted using multi-variate regression models.	-Single pollutant model: -Minn: for total respiratory admission, ozone lag 1 d, 15 ppb increase was associated with 6% (95% CI 3.3-8.7%) increase in admission. -Birm: for total respiratory admission, ozone lag 2 d, 15 ppb increase was associated with 0.27% (95% CI –0.2 to 0.74%) increase in admission, not significant. -Multivariate models: -Minn: for total respiratory admission, ozone lag 1 d, 15 ppb increase was associated with 5.15% (95% CI 2.36-7.94%) increase in admission; for pneumonia, 6.6% (3.4-9.8%) increase; for COPD, 4.5% (-0.5% to 9.5%) increase. -Birm: 0.27% (-0.2% to 0.74%) increase, not significant.

Table 12.2a Ambient ozone and association with hospitalizations

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Anderson et al., 1997 Europe: 6 APHEA cities: Amsterdam (1977-1989), Barcelona (1986-1992), London (1987-1991), Milan (1980-1989), Paris (1987-1992), Rotterdam (1977-1989)	Hospital admissions for all ages: -COPD (ICD-9, codes 490,491, 492 and 496): A: 1.1/d B: 11/d L: 20/d M: 4/d P: 11/d R: 1.1/d The proportion of COPD admissions for patients aged ≥ 65 years ranged from 48% in Paris to 70% in Barcelona	O_3 1-h mean all year (converted from µg/m^3): A: 39.5 ppb B: 32.8 ppb L: 19.5 ppb M: - P: 18.5 ppb R: 36.4 ppb 8-h avg. all year (converted from µg/m^3): A: 35.2 ppb B: 28.6 ppb L: 14.3 ppb M: - P: 10.2 ppb Rotterdam: 31.1 ppb	SO_2 et NO_2: 24-h and 1-h max. means for each day TSP et BS: 24-h period Also monitored weather variables: temperature and relative humidity	-Daily counts of COPD admissions -Lag days 1,2,3 checked (up to 5 days for O_3) -Poisson regression analysis controlling for seasonal and other cycles; influenza epidemics; days of the week; temperature and humidity -autocorrelation checked	-Significant association between ozone and hospital admissions for COPD -For all ages, the relative risk (RR: 95% CI) for a 50 µg/m^3 (25.5 ppb for ozone) increase in mean level of pollutants (lagged 1 day) were: -SO_2: 1.02 (0.98, 1.06) -BS: 1.04 (1.01, 1.06) -TSP: 1.02 (1.00, 1.05) -NO_2: 1.02 (1.00, 1.05) -O_3 (8h): 1.043 (1.022, 1.065) lag one day; 1.056 (1.027-1.086) for 5 cumulative days. -O_3 (1 h): 1.029 (1.011, 1.047) lag one day; 1.049 (1.024-1.075) for 5 cumulative days. -For 8-h avg. ozone, RR cool season 1.03 (1.00-1.07), warm season 1.04 (1.02-1.07). For 1-h max. ozone, RR cool season 1.01 (0.98-1.05), warm season 1.03 (1.01-1.05).

Table 12.2a Ambient ozone and association with hospitalizations

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Schouten et al., 1996 Europe : 2 APHEA cities in the Netherlands: -Amsterdam (pop. 694,700) -Rotterdam (pop. 576,200) 1977-1989	Hospital admissions: -Respiratory A: 6.7/d R: 4.79/d) -COPD A: 1.74/d R: 1.57/d -Asthma: A: 1.13/d R: 0.53/d	converted from $\mu g/m^3$: O_3 8-h mean: -for May-Oct. (5-95%): A: 44.1 ppb (14.3-77.6); R: 42 ppb (12.8-81.1) -for whole year: A: 35.2 ppb (2.55-68.4 ppb); R: 32.6 ppb (3.1-71.4). O_3 1-h max.: -for May-Oct.: A: 49.7 ppb (21.4-88.3); R: 49.2 ppb (18.4-94.9). -whole year: A: 40.3 ppb (5.1-77.0); R: 38.8 ppb (5.6- 83.7)	SO_2: 24-h period (mean of all year) A: 28 $\mu g/m^3$ R: 40 $\mu g/m^3$ BS: 24-h period A: 11 $\mu g/m^3$ R: 26 $\mu g/m^3$ NO_2 :24-h period A: 50 $\mu g/m^3$ R: 54 $\mu g/m^3$	-Daily number of admissions for the three classifications -Poisson regression model with and without autoregressive terms -Dummy variable for the winter and its interaction with the pollutant was included in the model with a dummy variable for the summer and the pollutant	-No correlation with summer O_3 8-h and respiratory admissions in people aged > 65 years in Amsterdam (RR=1.127, 95% CI 0.983-1.292, 1-d), but a significant positive association in Rotterdam (in 1977-81, RR=1.344, 95% CI=1.097, 1.647, in 1982-89, RR=0.950, in 1985-1989, RR=1.05) for a 100 $\mu g/m^3$ (51 ppb) increase in O_3 8-h. -1-h max. ozone, summer, 1-d: in Amsterdam, respiratory admission, age 15-64 y, 0.976 (95% CI 0.876- 1.088), age 65+ 1.109 (95% CI 0.987- 1.247); COPD: 1.049 (95% CI 0.923 - 1.193); asthma: 0.995 (0.834 – 1.186), for 51 ppb increase. -1-h max. ozone, in Rotterdam, summer, 1-d: respiratory admission, age 15-64 y, 1.026 (0.940– 1.120); age 65+, 1.346 (1.133- 1.598)(in 1977-1981); COPD, 1.038 (0.927 -1.163) , for 51 ppb increase. -SO_2 and NO2 did not show any clear effects in Amsterdam and Rotterdam -BS did not show any clear effects in Amsterdam; in Rotterdam it was positively but not significantly related to the number of admissions

Table 12.2a Ambient ozone and association with hospitalizations

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Ponce de Leon et al., 1996 London (pop. 7,300,000) April, 1987 to February 1992	Respiratory admissions (ICD-9, 460-519), all ages separated into categories: -0-14y:45.4/d -15-64y:33.6/d -65+ y: 46.7/d	O_3 8-h mean: Whole year: 15.6 ppb (10-90% 3-29 ppb); summer 7-36 ppb. O_3 1-h max: 20.6 ppb (5-95% 2-46 ppb) Only 4 monitored stations with moderate correlation between them (data not given)	Other pollutant measured as an daily average: BS: 14.6 $\mu g/m^3$ SO_2: 32.2 $\mu g/m^3$ NO_2: 37.3 ppb	-Poisson regression analysis, adjusting for effect of trend, seasonal and other cyclical factors, day of the week, holidays, influenza epidemic, temperature, humidity. -Autocorrelation check -Same day and lagged 1,2,3 were checked	-O_3 (lagged one day) was significantly associated with an increase in daily admissions among all age groups, except for the 0-14y -This effect was stronger in the "warm" season (April-September) -Very few significant associations were observed with the other pollutants -In summer the RR (95% CI) in 8-h O_3 levels of 29 ppb were (single pollutant models): 1.0483 (1.0246, 1.0726), all ages 1.0294 (0.9930, 1.0672), 0-14y 1.0751 (1.0354, 1.1163), 15-64 y 1.0616 (1.0243, 1.1003), >65 y --Whole year RR in 8-h O_3 levels of 26 ppb were (single pollutant models): 1.0293 (95% CI=1.0113, 1.0477), all ages 1.0269 (95% CI=0.9995, 1.0551), 0-14y 1.0536 (95% CI=1.0232, 1.0849), 15-64y 1.0455 (95% CI=1.0172, 1.0746), 65+ y. -1-h max. ozone effects effects (RR 1.00084/ppb, SE 0.000282/ppb, p<0.01) are smaller than effects of 8-h avg. ozone. Threshold for 1-h ozone may be at 40 ppb. -Whole year ozone (8-h, 26 ppb) + other pollutants models, RR±SE: 1.0292 ±0..0091, +NO_2 1.0292 ± 0.0091, + BS 1.0285 ± 0.0091, +SO_2

Table 12.2a Ambient ozone and association with hospitalizations

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Burnett, 1998 (Special analysis for WGAQOG) 13 Canadian cities (pop. 10,800,000) April 1, 1981 to December 31, 1991	Daily number of admissions to hospital (respiratory diseases) for: -Acute bronchitis (ICD-9, 466) -Pneumonia (ICD-9, 480-486) -COPD (ICD-9, 490-496)	O_3 1-h max: 31 ppb Range: (25-38 ppb) Data were average over all stations in each cities (data not given)	Also monitored: daily readings of maximum and minimum temperature, daily average dew point temperature and daily average relative humidity Even Rate/Day for admissions: 13.0	-Estimation of a "National Reference Level" for ozone in Canada date -Number of daily admissions rates for respiratory diseases -Poisson regression analysis were both the respiratory admissions data and the daily variations in 1-h maximum O_3 levels were adjusted using pre-filtered non-parametric smoothed functions of day of study and day of the week differences for each cities - O_3 levels recorded same day and lagged 1,2,3,4 day prior to the event	-Single pollutant model, increase of hospitalizations for 10 ppb ozone: 1.04% (95% CI 0.78-1.30%). -This risk tended to decrease slightly if ozone values above 25 ppb are not included in the analysis (0.74%) -The risk is clearly reduced if days above 20 ppb are excluded -Risk of respiratory admissions increases from 0-2 days lagged and then decreased to 4 days lagged -The LOAEL is 25 ppb based on respiratory admissions (0.74%) -Evidence of a threshold between 15 and 20 ppb

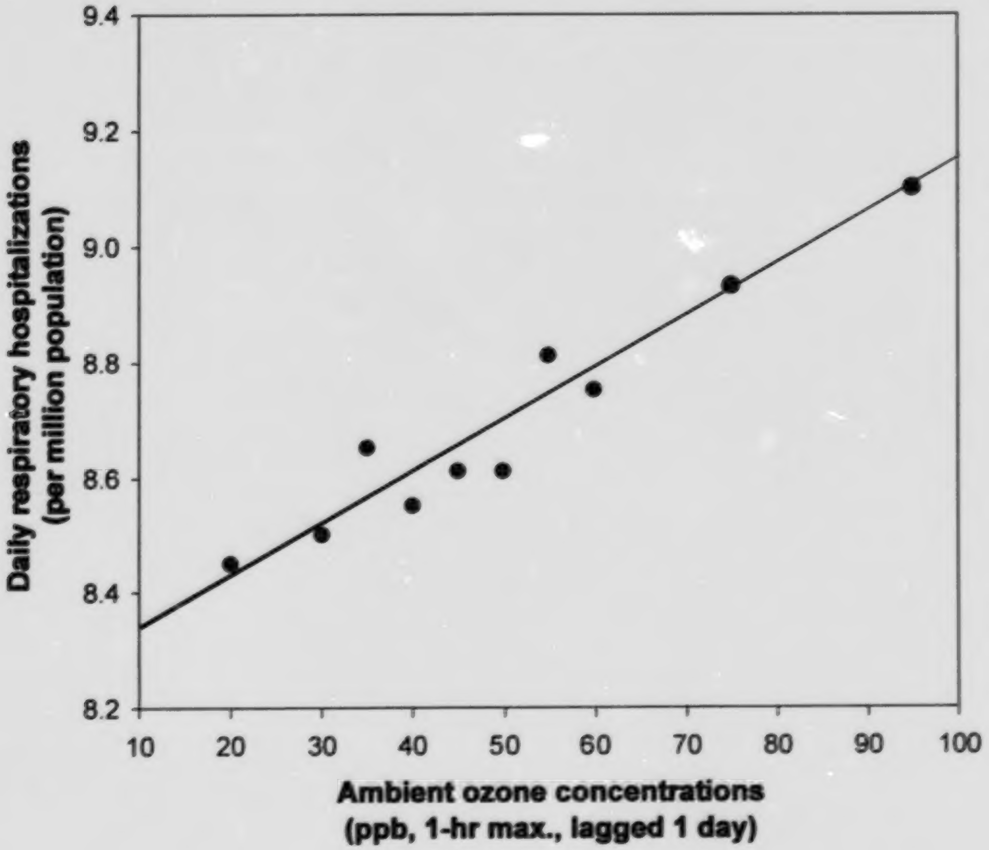
12.3.1 Canadian studies

Two recently completed large scale Canadian studies investigated the effect of short-term high ozone concentrations on respiratory morbidity, utilizing hospital admissions as an objective measure. In a study which covered all of Southern Ontario (and a little of Northern Ontario–Sudbury, Algoma) and included data from a population base of 8.7 million people over a period of 6 years (1983-88), a small but statistically highly significant association ($p= 0.001$) was found between one-hour peak ozone concentrations recorded the previous day and respiratory hospital admissions during the summer months of May-August (Burnett et al. 1994). An independent increase of 5.0% of admissions was associated with an increase in ozone from 0 to 50 ppb, based on a model which included temperature and sulphates as covariates. The relationship was also significant, but somewhat weaker, for 1-h ozone concentrations recorded the same day, or lagged by two or three days, but was not significant for concentrations recorded four days previously. Sulphates (lagged one day) were also independently associated with hospital admissions, accounting for a further 1% (based on a 5.3 $\mu g/m^3$ level). There were no associations between a control group of non-respiratory hospital admissions and any of the three main variables, i.e. ozone, sulphate or temperature.

The data from the Southern Ontario study do not provide any evidence of a threshold for the effects of either ozone or sulphates (Burnett et al., 1994). The concentration-response relationship appeared to be linear at all concentrations. Figure 12.1 shows the hospitalizations observed in the Ontario study compared to ozone levels (lagged one day)(reproduced from Burnett et al. 1994). A similar graph for sulphates was also published.

In this study (Burnett et al., 1994), each hospital acted as its own control, and 91% of the independently calculated hospital-specific relative risks for increased admissions due to ozone were positive (Relative Risk range = 0.96-1.24 for a 50 ppb increase). The association with sulphates was positive for all 168 hospitals (RR=1.003-1.035 for a 5 $\mu g/m^3$ increase in sulphates). The associations were thus consistent across the entire study region, which included Canada's largest city and metropolitan area as well as large rural and forested areas, some of which were not affected by transboundary transport of air pollution.

Figure 12.1 Association of respiratory admissions in Ontario with ozone pollution (source: Burnett et al., 1994).



The association between ambient ozone levels and hospitalizations was manifested in spring, summer and fall, when ozone concentrations peaked, but was not the case for winter (Burnett et al., 1994). Ozone concentrations were generally low, with the average of 1-h peak concentrations less than 40 ppb for all months except the four months May–August. During summer (May-August), the overall average for the 22 monitoring districts was 52 ppb (range 32-70 ppb) and the 95th percentile was 92 ppb (range for the 22 districts 62 to 118 ppb). Other ozone metrics than the 1-h daily maximum was considered in this study, but the 1-hour maximum was chosen. This was because 1-hour maximum ozone were consistent with other previous studies in the same area (Bates & Sizto, 1987; Thurston et al., 1992, 1994a,b), and it was highly correlated with the 8-h daytime average and with the 24-h average (Pearson correlation coefficient 0.99 and 0.87, respectively).

Respiratory admissions were subcategorized (using ICD9 Codes) for asthma, COPD or chronic obstructive pulmonary diseases (bronchitis, emphysema, bronchiectasis, chronic airway obstruction) and infection (acute bronchitis, bronchiolitis, pneumonia). Upper airway respiratory admissions were not considered. All three categories of respiratory admissions were shown to be significantly increased by air pollution (ozone plus sulphates), at 7% for asthma, 6% for COPD and 4% for infections, the latter being significantly increased only for infants.

Of the three categories, asthma was the most significantly affected ($p<0.001$). Interestingly, although the 2-34 years age group is often most affected by asthma without a concomitant high prevalence of COPD, only 5.5% ($p<0.05$) of asthma in this age group could be associated with air pollution (ozone plus sulphates). The association with asthma was strongest in the 35-64 years age group (10%, $p<0.001$), and was also significant in infants aged 0-1year at 13% of respiratory admissions for asthma ($p<0.05$), but was not significant for the elderly. Almost 6% of total COPD admissions could be associated with air pollution ($p<0.01$). As expected, COPD admissions were significantly associated in the elderly at 6% ($p<0.01$), but a 24% increase ($p<0.05$) was also observed for the 2-34 years age group. The COPD increase was not significant for the 35-64y age group, although it would be expected due to the development of chronic conditions (such as smoking-related diseases) as people age. This, coupled with the anomalies noted above in admissions for asthma in the same two age groups, raises the question of misclassification of the respiratory subcategories due to inaccurate discharge diagnosis.

Admissions were also categorized by age into four groups: <2 years (12% of admissions), 2-34 years (30%), 35-64 years (22%), and 65+ years (36% of admissions). Significant increases in overall respiratory admissions due to ozone were seen in all age groups, but were most marked in infants, with 15% of their admissions calculated to be due to ozone ($P<0.001$). This is most likely due to increases (19%, $p<0.001$) in infections, but partly also due to asthma (13.0% increase, $p<0.05$). The air pollutant effect was least marked in the elderly (4.3% ascribed to ozone plus sulphate), due to a significant increase (6.0%, $p<0.01$) in COPD diseases, as expected for this age group. The calculated increases due to air pollution in the other two age groups (5.5% and 7.2% for ages 2-34y and 35-64y respectively) were close to the overall average of 5.8% (5.0% for a 50 ppb increase in ozone and 0.8% for a 5.3 $\mu g/m^3$ increase in sulphate).

Multiple regression and a rigorous but conservative statistical treatment for random non-Gaussian (non-normal) effects were used to investigate the relative risk of increased hospitalizations due to ozone and sulphates, taking temperature into account. Long-term cyclic seasonal variations in the data for both hospitalizations and independent variables were detrended by using a 19-day weighted moving average, leaving only short-term variations to be examined. Terms were included for differences in admissions between days of the week, and for inter-hospital differences due to factors such as different admission rates for small community hospitals versus large teaching hospitals. Serial correlations were examined but were not found.

Exposure to ozone was estimated by 22 ambient monitors over the entire area (approximately 800 km east to west, 5° of latitude, 42° to 47° or 550 km south to north), and the area was divided so that each monitor was representative of its own area. Pairwise correlations among the 22 monitoring stations showed a high degree of correlation (>0.68) between ozone values from stations 100 km or less apart. This is likely due to the nature of the circumstances producing ozone in southern Ontario, most of which is due to long-range transport from distant regions (Burnett et al., 1994). Therefore, ambient concentrations within each region were considered to be quite homogeneous spatially, and each regional monitoring station to represent quite accurately the ambient concentrations to which people entering all hospitals in the region were exposed. Exposure misclassification due to placement of the ambient monitors was not therefore very likely, and any misclassification would have arisen because of differences in activity patterns and indoor exposure. Concentrations from ambient monitors must correlate with concentrations from personal exposure monitors, if there is to be confidence that ozone concentrations measured at ambient monitors can be considered representative of population exposures. However, they do not need to be (and are not) the same. This correlation has been demonstrated in several Canadian and US cities (see Chapter 6 for detail). Indoor ozone levels tend to approximate outdoor levels most closely during summer when windows are open. In addition, many people tend to spend more time outdoors in summer.

Potential confounding factors were well handled in the study by including them into the regression analysis where possible, and by providing semi-quantitative estimates of their importance if they could not be included. Daily temperature was known to be independently predictive of hospitalizations, and was also moderately correlated with ozone (r=0.55, range 0.41 to 0.67). It was therefore a potential confounder, and was included in all regressions as the daily mean [which was correlated to the daily maximum temperature (r=0.95)]. Average relative humidity was weakly correlated with ozone (r=-0.17) and with sulphate (r=0.12), while average barometric pressure was not (r=0.03 for ozone and r=0.00 for sulphate). They were therefore dropped from the analysis.

The analysis of other covariates and potential confounders focused on particles since previous work had consistently shown them to be related to hospital admissions. The sulphate fraction of fine particles is even more homogeneous over southern Ontario than ozone, due also to long range transport, and 9 monitors therefore adequately characterized exposure. Daily estimates of exposure to particulate matter or particulate acid levels (as H^+) were not available for most of the province and could therefore not be included in the analysis. However, analyses of the relationship between inhalable particulate matter (as PM_{10}), fine particulate matter (as $PM_{2.5}$), excess H^+, and sulphates in northeastern North America showed them to be highly correlated with each other in the summer (>0.80) (Dann, 1994). Personal monitoring for sulphates have also been shown to be highly correlated with monitoring results from fixed site central monitors (R^2=0.9, Stieb et al., 1998), and more highly correlated than PM_{10} (Clayton et al., 1993). In addition, sulphates, being in the small size fraction of particulate matter, readily infiltrate indoors where the majority of time is spent for most people, thus ensuring that everyone is exposed. Indoor sources for sulphate are minimal. In a study on air pollutants and hospitalizations in Toronto, Thurston et al. (1994a,b) made several direct comparisons between different measures of particulate matter as covariates with ozone in associations with hospitalizations. Sulphate was a better predictor than fine mass, and much better than PM_{10}. The inclusion of sulphate in the Ontario analysis is therefore considered to be a good surrogate for exposure to particulate matter and acidity for southern Ontario in the 1980s (although it might not be so suitable in other locations or at other times, when the correlations might not be so strong). The effects of sulphate and ozone were additive, and sulphate reduced the association of hospitalizations with ozone only slightly (from 5.1%, reduced to 4.6%), while ozone halved the association with sulphate (from 2.2%, reduced to 1%) when each was regressed including the other.

Daily SO_2 and NO_2 readings were also obtained from 24 and 18 monitoring sites respectively, but correlations between sites were lower than 0.4 (SO_2) or 0.5 (NO_2), indicating that not enough monitoring stations were available to provide accurate exposure estimates for each of the 168 hospitals. Therefore, these two factors could not be included in the regression. Neither SO_2 nor NO_2 was considered to be a strong confounder for ozone or sulphate, since the correlations between ozone and daily maximum SO_2 (r=0.20) or NO_2 (r=0.29) were quite low, and the correlations for sulphate with SO_2 (r=0.16) and NO_2 (r=0.30) were also relatively low.

The second Canadian study (Burnett et al. 1997a) involves an even more extensive area covering 16 cities in all populated regions across Canada, representing 12.6 million people, or about half the population of Canada in the years (1981 to 1991) of the survey. All cities with a population of over 100,000 for which monitoring data were available were included; from the Pacific coast to the Atlantic they were: Victoria and Vancouver (B.C), Edmonton and Calgary (Alta.), Regina and Saskatoon (Sask.), Winnipeg (Man.), Windsor, London, Hamilton, Toronto, and Ottawa (Ont.), Montreal and Quebec City (Que.), St. John (N.B.), and Halifax (N.S.). Respiratory admissions were not broken down into subcategories, nor were subclassifications by age examined, as they had been in the Ontario study. Multiple regression was carried out as in the previous Ontario study (Burnett et al., 1994), using a 19-day weighted linear filter to detrend seasonal cyclic variations, dummy variables for hospital effects, day to day variations, location, and weather.

After simultaneous adjustment for CO and dew point temperature, RR of increased respiratory hospitalizations during spring, summer and fall for an increase in the daily 1-h maximum ozone (lagged 1 day) of 30 ppb (close to the mean) was 1.043 ($p<0.0001$) for all 16 cities. Only 11 cities had data of CoH (a PM index) available, and were used to adjust for PM effects. RR of respiratory hospitalizations for 30 ppb ozone was 1.024 ($p=0.026$) for these 11 cities with CoH, CO and dew point temperature in the model. There was no evidence of an association between ozone and a control group of non-respiratory hospital admissions for certain blood diseases and diseases of the nervous, digestive and genitourinary systems. This negative result suggests that the ozone association was not due to factors influencing admission to hospital in general.

The association between ozone and respiratory hospitalizations was similar for those patients older than 65 years of age (RR 1.040 for a 30 ppb increase, 95% CI: 1.010-1.072) representing one-third of admissions, and those patients younger than 65 years of age (RR 1.045, 95% CI: 1.021-1.068). This result suggests that the elderly are not the only people who are at risk for ozone episodes.

This increase in relative risks was seen for all cities except Montreal and Vancouver (RR=1.000 and 1.003 respectively, adjusted for dew point temperature and CO). Other city-specific relative risks varied from 1.021 (Calgary) to 1.069 (Regina). Several possible reasons for the lack of association in Montreal and Vancouver between admissions and ozone were explored. Adjustment for CoH made little difference. The Pearson correlation coefficients between ozone and dew point temperature were 0.29 for Montreal and 0.23 for Vancouver, similar to the study mean of 0.23, and therefore not high enough to suggest that this could be the cause of the non-significance. The unadjusted ozone relative risks were also low, but the reasons for such a weak ozone effect remain unclear. Other authors have found a similar lack of association for these two cities; Emergency Department visits for asthma in Vancouver were examined by Bates et al. (1990) and hospitalizations in Montreal were studied by Delfino et al. (1994).

The observations of lower risk of hospitalizations in Vancouver and Montreal (Burnett et al., 1997, delfino et al. 1994) than other Canadian cities are in line with the exposure data using the probabilistic National Exposure Model (pNEM, see Chapter 6.3.3). The pNEM study has demonstrated that when time-activity patterns and microenvironment ozone data were incorporated for population exposure estimates, Vancouver and Montreal had much lower population exposure levels of ozone than Toronto.

The effects of four sampling times were also considered, but the daily 1-hour maximum concentration of ozone was statistically the most significant factor explaining the excess hospitalization rate compared to the daily average, average 8am-8pm (daytime) concentration, or maximum 8-h running average. Also the 1 day lagged concentration was more predictive than the concentration on the day of admission (day 0) or that of two days previously. Concentrations averaged over lagged days 0 and 1, days 0,1,and 2, and days 1 and 2 were also tested, but were also not as strongly associated as concentrations at lag day 1.

Ozone concentrations were low in all cities in comparison to the current objective of 82 ppb. For the spring-summer period when ozone levels are usually highest and a significant correlation with hospitalizations is most likely to be observed, the 16-city ozone mean and 95th percentile values based on the 1-hr daily maximum were 33 and 64 ppb, respectively. As observed previously, there was no increase in relative risk in winter when ozone levels were low (RR = 0.993), and the increase was highest in summer when ozone levels peak, (RR=1.043; 95% CI:1.021-1.066).

Daily maximum and minimum temperatures as well as dewpoint temperature, all of which were highly intercorrelated, were also examined, but the dew point temperature was selected for inclusion in the regressions as a potential confounder, since associations were judged to be strongest using this metric.

Four additional pollutants were considered as potential confounders. Although particulate matter had been shown in other studies to be an important covariate predictor of increased hospitalizations (for both respiratory and cardiovascular conditions), daily measures of particulate matter including sulphates, were not available for most of the cities in the study. Soiling Index (as CoH) is related to particles and was used as a substitute for 11 of the 16 cities. No CoH measurements were available for 5 cities, and they were not included in the analysis for particulate matter. The ozone RR for hospitalizations was reduced to 1.024 ($p=0.026$) for these 11 cities, adjusting for dew point, CO and CoH. CoH may be a less satisfactory surrogate for particulate matter than sulphate, based on results from several of the mortality studies. However, the weakness of the particle effect, as measured by sulphate in the Burnett et al. (1994) study in southern Ontario, and by sulphate, fine mass and PM_{10} in the Thurston et al. (1994a,b) study in Toronto, gives some assurance that the lack of a good particle surrogate in the national study was not an important source of confounding. There was little evidence of an association between respiratory hospitalizations and either NO_2 ($p=0.77$) or SO_2 ($p=0.13$) and they were dropped from the multiple regression analysis.

Two other Canadian studies conducted by Burnett et al. (1997b,c), though focusing on PM (1997b) or carbon monoxide (1997c) rather than on ozone, provided additional evidence for ozone effects on respiratory hospitalizations. In the study by Burnett et al. (1997b), the researchers investigated the effects of various PM metrics and ozone on respiratory and cardiac hospitalizations in Toronto between 1992-1994. The authors found that the adjustment for temperature did not affect the ozone-cardiorespiratory associations, RR for respiratory admissions was 1.064 ($p<0.05$), and for cardiac admissions was 1.074 ($p<0.05$), for a 11.5 ppb increase in ozone. No multi-pollutant regression was conducted for ozone, while for PM after the adjustment of gaseous pollutants, PM_{10}, $PM_{2.5}$, sulphate and H^+ still revealed a significant association with cardiac and respiratory admissions. The correlation coefficients of ozone with PM metrics were between 0.20 (coarse particles) and 0.53 (sulphates), and were minimal with other gaseous pollutants (r between 0.02-0.18). Thus the ozone-hospitalization associations would have been more convincing if PM effects had been adjusted during the regression analyses.

In the study by Burnett (1997c), the study focused on CO effects on congestive heart failure in the elderly (>65 years of age). While the authors detected a significant association between CO and congestive heart failure even after adjusting for PM, and other gaseous pollutants, the effect of ozone was moderately significant. When controlled for temperature, log-RR coefficient was 0.0022 (t ratio=1.8); when controlled for temperature and all the other pollutants, log-RR coefficient=0.0021 (t ratio=2.0). This is not surprising, since other than in the study by Burnett et al. (1997b), ozone has not been documented to be associated with cardiac hospitalizations.

The results of the Ontario and the 16-Canadian city studies are quite consistent within each study, with each other and with the results of other time-series studies published in the past few years. Burnett et al. (1994,1997a) found virtually the same relative risk of 1.032 and 1.033 for respiratory hospitalizations due to ozone in the Ontario and in the national study. The Ontario study (Burnett et al., 1994) confirmed and extended the findings from a previous series of studies by Bates & Sizto (1987, 1989).

Following a request from the WGAQOG, Dr. R. Burnett revisited the above 2 Canadian studies, and performed a regression analysis using the data from 13 cities (Vancouver, Edmonton, Calgary, Winnipeg, Windsor, London, Hamilton, Toronto, Ottawa, Montreal, Quebec City, Saint John, and Halifax). The data were analyzed for both hospitalization and mortality endpoints using single-variate models. The actual methods and results of the analysis are provided in Appendix A (Burnett, 1998). The regression analysis showed that the ozone risk associated with hospitalization for respiratory diseases is 1.04% per 10 ppb increase in daily one hour maximum ozone (95%CI: 0.78-1.30%). The lowest observable adverse effect level (LOAEL) with statistical significance, derived from the data, is 25 ppb ($p<0.01$). Interestingly, the data show that the regression coefficient between ozone and hospitalization becomes negative between 15 and 20 ppb indicating a possible threshold for hospitalization based on the result of this new analysis.

An earlier study by Bates and Sizto (1987, 1989) covered a smaller area of southern Ontario than the 1994 study, and included 5.9 million people and data for nine years, 1974 and 1976-83. The analysis was confined to short two-month seasons, winter (January-February) and summer (July-August) in order to reduce cyclic seasonal variations in admissions. Longer term (multi-year) downward trends in some pollutant levels necessitated analysis of each year separately. Day-to-day variation in hospitalizations was shown to exist, and was handled by comparing only same-day (e.g., Tuesday) hospitalizations within the same 2 month period and same year to the pollution variable (lagged 0-4 days).

During summer (July and August), a significant association ($p<0.001$) was found between total respiratory hospital admissions and 1-h peak ozone levels (lagged 1 or 2 days). Ozone was also correlated with respiratory admissions minus asthma (lagged 2 days only) and with all-age asthma admissions, but not with asthma in children aged 0-14 years. Sulphate (SO_4) and sulphur dioxide (SO_2) were also correlated to the same three endpoints with about the same lag times for SO_4 and a lag of 2 days only for SO_2. Surprisingly, coefficient of haze (CoH) was not correlated to any of the respiratory categories. There were no correlations of any air pollutant with a control group of non-respiratory diseases or conditions. In winter, correlation analysis between temperature, pollution factors, and hospitalizations showed that only temperature (lag 0,1,2 days) was correlated with total respiratory visits and asthma admissions for all ages including children aged 0-14 y (Bates & Sizto, 1987).

In summer, cross-correlation analysis indicated that all air pollutants plus temperature were highly correlated with ozone, with coefficients >0.6, except CoH at 0.49 and humidity at 0.003 (Bates & Sizto, 1987). Temperature was included in a multiple regression, which indicated that ozone, sulphate and temperature together, all lagged 0,1,2 days, accounted for 5.6% of variability in respiratory admissions. If temperature was forced into the regression first, it only accounted for 0.9% of the hospital admissions. Addition of SO_4 and ozone accounted for an additional 2.4% and 2.3% respectively (Bates & Sizto, 1989).

The Bates and Sizto (1987) study provided evidence that asthma is not the only condition that appears to be affected by ozone; the association remained significant for respiratory admission minus asthma, although the latter comprised about 50% of all summer respiratory admissions. The asthma admissions of children who have been suggested as a target group for toxicity of ozone, did not show a significant association with ozone. However, Burnett et al. (1994) compared the Bates & Sizto results to theirs in a separate analysis using their more extensive database and a more rigorous statistical method of analysis. They were able to show a positive association between ozone and hospital admissions for children aged 0-14 years, with an 8.2% increase in asthma admissions per 50 ppb ozone (p=0.005) (Burnett et al., 1994). The increased statistical power to detect this effect may have been due to the larger number of admissions (approximately 50% more admissions) in the study by Burnett et al. (1994) compared to that of Bates and Sizto (1987) and the method of statistical analysis.

Bates & Sizto (1989) pointed out several anomalies in the hypothesis that ozone is the agent responsible for the increased hospitalizations; in their data these included a lack of demonstrable effects on hospitalizations in June 1983 when ozone was consistently >82 ppb compared to the same period in 1982 when ozone was lower on average, and a lack of correlation for daily SO_4 at one central monitoring station when values for all monitors, collected every sixth day, were correlated with hospitalizations. They concluded that probably neither ozone nor SO_4 alone was responsible for the observed associations with acute respiratory admissions, and suggested that acidity (H^+ ion) was a good candidate as a potentiator of the ozone/sulphate effect.

It is noteworthy that the earlier Southern Ontario studies (Bates & Sizto, 1987) treated the whole area as one entity from the point of view of exposure. If ozone concentrations were not homogeneous in this area, then this may cause misrepresentation of exposure. This generalization of exposure also gave significant Pearson coefficients for ozone and SO_4, which might artificially weaken the potential effect of ozone. Burnett et al. (1994) refined the exposure data by using the ozone monitor closest to the hospital in which the admissions were being recorded, which reduced the chance of misclassification of exposure. This resulted in an increase in the significance of the association between ozone and admissions. Zidek's recent calculations (1996) of individual exposure of people admitted to hospital for respiratory conditions based on the census code of the admitted individual and a system of "kriging" to compute probable ozone ambient exposure has added another order of magnitude to the level of data accuracy and significance found. The demonstrated increase in significance of the association as the exposure calculation is refined and improved, constitutes a powerful argument for causality.

Thurston et al. (1994a,b) examined the relationship of total respiratory and asthma hospital admissions in Toronto, Ontario, with ozone and fine particles, represented by sulphate and acidity as H^+ ion, during July and August 1986-88. After detrending the hospitalization, pollutant and temperature data, as well as controlling for day-of-the week effects, bivariate correlation analyses were carried out. Ozone was highly correlated ($r>0.6$) with SO_4, NO_2, and maximum temperature, while correlations with H^+ and SO_2 were moderate (0.51 and 0.41 respectively). As expected, the measures of fine particles H^+ and SO_4 were highly correlated with a coefficient of 0.81. The correlations between total respiratory or asthma-related admissions and ozone, SO_4 or H^+ were relatively weak, and all in the same range, 0.21-0.28, while correlations with SO_2, NO_2 and maximum temperature were all low, 0.2 or less. SO_2 and NO_2 were therefore dropped from the regression analysis, and simultaneous regression of temperature with each of ozone, SO_4 and H^+ in turn yielded independent relative risk (RR) estimates for respiratory and asthma-related hospitalizations.

Results from Thurston et al. (1994a,b) reveal strong associations between summer haze pollution (i.e., ozone, H^+ and SO_4) and total respiratory or asthma hospital admissions on the same or following days. For ozone, the RR was calculated to be 1.36 (95% CI 1.13-1.59) per 100 ppb ozone. For SO_4, the RR was 1.30 (95% CI 1.07-1.53) and for H^+, the RR was 1.25 (95% CI 1.06-1.44). Paired regressions were carried out between ozone, SO_4 and H^+ as well as fine particles (FP), PM_{10}, TSP, and the fraction of TSP above PM_{10} in size. Ozone remained highly significant as a predictor of respiratory hospitalizations with either SO_4 or H^+ in the model ($p=0.008$ in each case). The regression coefficients for ozone remained almost the same, while the coefficients for H^+ and SO_4 were reduced by one fourth to one third, and, in the case of SO_4, was only marginally significant. The coefficients dropped for all the ozone-PM metrics, but that for ozone remained significant with FP, and marginal with TSP and TSP-PM_{10}. Because of the high correlation coefficients of ozone ($r=0.64-0.75$) with all the particle metrics, their effects on hospitalizations could not be separated from each other. The correlation coefficients for O_3-H^+ was relatively moderate ($r=0.51$), thus allowing the authors to conclude that the adverse effects of H^+ on respiratory hospital admissions are real. The authors calculated the overall pollutant mean effect to be about 9% for the summertime haze combination of ozone, SO_4 and H^+, by averaging the individual pollutant mean effects of 19.9% for ozone, 5.6% for sulphate and 2% for acid H^+. Thurston and colleagues concluded that there was no clear discrimination of a single pollutant as the responsible agent, but the regression results suggest that ozone was the summertime haze constituent of greatest relevance to hospital admissions. The authors also postulated a potentiating role for high H^+ concentrations in combination with ozone.

Concentration-response relationships were examined by categorizing data into quartiles for temperature, ozone and acid H^+ and plotting against total respiratory admissions (Thurston et al., 1994a,b). In the case of ozone, admissions were equally increased for the two highest quartiles at 60 and 90+ ppb, while there was no increase in the two lower quartiles, in both filtered and unfiltered data. For aerosol acidity H^+, the mean admissions were increased only for the upper quartile, >80 nmole/m^3. The filtered 1-h maximum temperature was the only one of the three to display a linear relationship with admissions, for the range 22-37^{0}C. The slope of the regression curve was also examined by means of a sensitivity analysis for evidence of changes in slope with concentration. The slope for total respiratory admissions for all 117 days was 0.051 admissions/ppb ozone. It decreased slightly to 0.048 when the two days >120 ppb were removed, and to 0.045 when all days above 80 ppb (N=22) were removed. The monotonically increasing linear dose-response with ozone seen in the Burnett et al. (1994) study in southern Ontario was thus not observed here. However, the Thurston study encompassed only metro Toronto, with a population of 2.4 million versus 8.7 million for the southern Ontario study (Burnett et al., 1994), and included only three 2-month periods compared to 9 years, with 4 months each year.

Thurston and colleagues presented an interesting comparison of lag effects, both negative and positive, between their Toronto data and Buffalo data (Thurston et al., 1992), concentrating on 1988, when hot hazy weather conditions were especially prevalent. Buffalo is 60 miles south west of Toronto and has a similar climate. It is reasonable that some time might elapse between the time of highest ambient pollutant level and the time that affected individuals are admitted to hospital. In both studies, and in others as well, this lag is observed. Admissions were also tested against a negative lag, i.e., pollutant levels 1-4 days after the hospitalization events. The lag effects were always in the expected direction for both respiratory and asthma visits correlated with ozone, SO_4, H^+ or temperature, but were randomly distributed for the control group of non-respiratory diseases. The proper temporality of the association was thus strongly evidenced. Lag times were 0-2 days for Toronto, with the lag of 1 day most highly correlated in the cases of ozone, H^+ and SO4, and 2 days for temperature. Lag times were slightly longer for Buffalo, 0-3 days with lag 2 days most highly correlated with ozone. These minor differences are likely due to differences in social or medical practices between the two cities.

Delfino et al. (1994) examined the relationship between the number of daily urgent hospital admissions for respiratory illnesses (31 hosptials) and ambient air pollution in Montreal, Quebec, during warm seasons between 1984 and 1988. A High-pass filter (19-d moving average) was used to eliminate yearly seasonal trends in the data. Day-of week trends were controlled by prefiltering the outcome variables prior to analysis. The authors used ordinary least-squares to regress single air pollutants on the outcome. They also tried to adjust for PM_{10}, sulphate and temperature by co-regressions with ozone. In summer (July and August), the results showed a statistically significant univariate association of all respiratory admissions to 8-hour average ozone. The association was substantially reduced when co-regressed with temperature. When adjusted for PM_{10} or sulphate, the associations of ozone (1-hour maximum) with asthma and with non-asthma respiratory admissions were nonsignificant. The correlations of ozone with PM_{10}, sulphate and temperature were high (r=0.68, 0.66 and 0.72, respectively), which may have contributed to the weakened associations between ozone and respiratory hospitalizations. These strong correlations also made it difficult to separate the effect of ozone from other environmental factors. These findings are consistent with those reported by Burnett et al. (1997a) who also found that the associations of ozone with respiratory hospitalizations in Montreal were weak when compared with other Canadian cities.

12.3.2 Studies in other areas

Thurston et al (1992) found the relative risk for total respiratory admissions in Buffalo, NY and New York City (based on the 1988 high-pollution summer) were 1.22 and 1.19 for ozone. However, the high inter-correlation between SO_4, H^+ and ozone prevented the authors from performing multi-variate analysis, and from singling out the specific contribution of ozone to the relative risk of hospitalization due to pollution episodes.

Schwartz has examined Birmingham, AL (1994a), Detroit, MI (1994b), Minneapolis, MN (1994c), New Haven, CT and Tacoma, WA (1995), and Spokane, WA (1996) with respect to possible association of hospital admissions in the elderly (>65 years) with ozone and PM_{10}. In Birmingham, AL (Schwartz, 1994a), although the relative risk for respiratory hospitalizations increased, it was not statistically significant (RR=1.14 for 50 ppb increase in ozone, 95% CI: 0.94-1.38). Several methodological deficiencies exist in this study, including no correction for day of the week effects and no adjustment for other atmospheric pollutants (SO_2, NO_2, PM_{10}) when compared with studies from other cities (Schwartz, 1994b,c, 1995), which may have precluded detection of a significant effect from ozone.

The correlation was significant for ozone and hospital admissions for pneumonia and chronic obstructive pulmonary disease (COPD) in elderly people in Detroit and for pneumonia only in Minneapolis (Schwartz, 1994 b,c). In these two studies, temperature and PM_{10}, two most marked confounders, were simultaneously adjusted in the analyses. In Detroit, ozone was estimated to be responsible for 11.3% of excess admissions for pneumonia and 12.2% for COPD (Schwartz, 1994b). In Minneapolis, after adjustment for PM and temperature, the RR was 1.22 (95% CI 1.02-1.47, for 50 ppb increase in ozone) for pneumonia (Schwartz, 1994c). The effect of PM_{10} was about half the ozone effect for pneumonia. There was no significant association of either PM_{10} or ozone with asthma. This is not inconsistent with the Burnett et al (1994, 1997a) studies, since asthma is expected to occur more frequently in younger people, and the number of daily admissions for asthma may have been too low for the elderly to provide meaningful results.

Moolgavkar et al. (1997) conducted a re-examination of the data from Minneapolis-St. Paul and Birmingham AL, with the addition of two more years of data. Semiparametric Poisson regression models were used for analyses of the data. Temperature and day of study, the latter to adjust for temporal trends and variations in hospital admissions not attributable to pollution or weather, were adjusted by nonparametric smoothers. PM_{10}, NO_2, SO_2 and CO were concurrently adjusted using multi-variate regression models. The reanalysis (Moolgavkar et al., 1997) confirmed Schwartz's results (1994a and 1994c), and concluded that a 15 ppb increase in ozone on the day before was associated with a 5% increase in respiratory admissions in the elderly (65+ years) in Minneapolis-St. Paul, but not in Birmingham. One explanation for the lack of associations in Birmingham is that the ozone data in winter were unavailable which limited the data size. An alternative explanation is that the results are sensitive to the form in which these covariates are entered into the model.

For New Haven and Tacoma (Schwartz 1995), respiratory hospital admissions were associated with SO_2, PM_{10}, and ozone, with ozone associated independently of the other pollutants. However, in New Haven, the association was marginal, with a relative risk of 1.07 (CI 1.00-1.15) when PM_{10} effect was adjusted. In Tacoma, the association of ozone with respiratory hospitalization was statistically significant both taken alone and after adjustment for PM_{10} ($p<0.005$ and $p<0.01$). The relative risk was higher than for New Haven, and was 1.20 (CI 1.06-1.37) for a 50 ug/m^3 (26 ppb) in mean 24-h ozone levels. The statistical analysis undertaken for the New Haven and Tacoma study was more comprehensive than the earlier analyses, and included use of a 19-day averaging period as a seasonal filter, and specific terms for each day of the week.

In Spokane (Schwartz, 1996), both PM_{10} and ozone were associated with an increased risk of respiratory hospital admissions in single-pollutant models. No multi-variate analysis was conducted because of too few days during which both measurements were taken (Schwartz, 1996). The RR for ozone (lagged 2 days) was 1.244 (95% CI 1.002-1.544) for a 26 ppb increase in ozone. This association remained significant when a two-dimensional smooth function of temperature and humidity was included, or when a smooth function of same-day and 4 preceding days' temperatures were included, but reduced to insignificance if the 5% of the days with the highest or lowest temperatures were removed prior to the analysis. This association is much higher than found by other authors, or by Schwartz in other studies, possibly because of the inability to control for particulate matter.

Anderson et al. (1997) investigated the data of ozone and hospital admissions for all age COPD from six European cities including Amsterdam, Barcelona, London, Milan, Paris and Rotterdam in the APHEA study. The authors found that both 1-hour maximum ozone and 8-hour average ozone, from both whole year and summer data, either one day before the hospitalization or 5 cumulative days, were significantly associated with all age COPD hospitalizations. Ozone in the cool season was not associated with COPD hospitalization. No multi-variate analysis was carried out in this study.

A separate analysis of respiratory hospital admissions in Amsterdam and Rotterdam found a significant association with 8-hr maximum ozone in Rotterdam but not in Amsterdam (Schouten et al., 1996). The reason for this was not explained. The results with 1-hr maximum ozone were almost identical to the 8-hr maximum ozone results. This study did not examine the confounding effects of other pollutants.

Within the same European project (APHEA) using the same methodolgy, in London (Ponce de Leon et al., 1996), the association of ozone (both 1-hour maximum and 8-hour average, summer and whole year) with all respiratory hospitalizations was significant in all age groups except in children aged 0-14 years. The authors also conducted multi-variate analyses and adjusted the effects of PM (BS), SO_2, and NO_2. After the adjustment for other pollutants, ozone remained significantly associated with all age respiratory hospitalizations.

Two authors, Thurston (1995) and Schwartz (1995) have attempted to present a summary of the magnitude of the effects on morbidity seen in these different studies (the unpublished Canadian study was not included in either). The information in the two summaries is not entirely compatible due to inclusion of slightly different sets of results, choice of different units of ozone measurement, and different ways of presenting the risk in the various studies. In Table 12.2b, we include all the available studies as of April 1997, including the latest Ontario (Burnett et al., 1994) and the 16-Canadian city study (Burnett et al. 1997a). Relative risks were standardized from the original units to a percentage increase in hospitalizations for a 10 ppb increase in ozone. The Table illustrates the results from single-pollutant or multi-pollutant models. These estimates encompassed southern Ontario, 16 cities across Canada, and 7 U.S. cities including one on the west coast. The lower end of the range was about 1.1, and this value is most likely to represent the "true" value since it is close to the values observed in the studies reviewing the largest and most diverse population database from different geographic areas in Canada.

12.3.3 Summary of ozone effects on hospitalizations (Table 12.2b)

Among the eighteen hospitalization studies reviewed in this document, sixteen of them have demonstrated statistically significant associations between ozone and respiratory hospitalizations in one or more aspects, using single-pollutant or multi-variate models. The aggregate results from time-series studies provide good evidence that environmental exposure to ozone at levels commonly encountered in Canada, the USA and European countries, perhaps in concert with other pollutants, is associated with adverse respiratory effects that are sufficiently severe to require hospitalization. This association has now been consistently observed in studies conducted in cities geographically spread across North America and Europe, differing in pollutant levels, components, population characteristics, and differing also in the statistical methods employed to take into account confounders, covariates and short- or long-term seasonal cycles in hospital admissions. The specificity of ozone has been shown in some studies where particle levels were low (Schwartz, 1995). In most of the studies that adjusted for the effects of temperature and other co-pollutants such as PM, ozone effects remained significant (8 out of 9 studies). It has been found that, if temperature is not included in the regression but rather prefiltered out, then some of the ozone effect is removed. The most common pollutant variables showing an inter-correlation with ozone were particulate matter, sulphate and acid haze (H^+ ion).

It is possible that hospitalizations due to the primary irritant action of ozone on the lung and respiratory system are exacerbated by one or more of these other environmental components, as proposed by Thurston (1994a,b) for acid haze (H^+).

Four studies compared the effects of ozone on different age groups. Two of these studies (Ponce de Leon et al., 1996, Burnett et al., 1997a) did not find that elderly people (>65 years) were more at risk than younger populations (<65 years), whereas one study (Schouten et al., 1996) found that only elderly people had a significant increase in respiratory hospitalizations following an ozone episode. One study examined the effects in 0-1 age group and found that infants appear to be most sensitive to the effects of air pollutants compared with other age groups. Therefore, very young people and the elderly are identified as the subpopulations potentially most at risk. This may include a substantial segment of the total population, estimated to be about 5% for diagnosed asthma, up to 20% if atopic individuals are included.

For hospitalizations, given the very diversified health endpoints and age groups in these studies, it is difficult to group the studies and conduct a meta-analysis for a weighted mean ozone effect. Thurston and Ito (1999)[4] in their latest publication presented a synthesis of ozone hospital admission studies. They grouped the estimates into four groups, and used the random effects model to obtain a combined weighted RR (95% CI) for each 100 ppb ozone (1-hour maximum) increase, for each group. The results are all from single-pollutant models:

(1) Canada/New York major respiratory admissions for all ages (Thurston et al., 1992,1994a,b; Delfino et al., 1994; Burnett et al., 1994,1997a,b), RR=1.18 (95%CI 1.10-1.26);

(2) Canada/New York asthma admissions for all ages (Thurston et al., 1992,1994; Delfino et al., 1994) RR=1.18 (95% CI 1.07-1.30);

(3) US Medicare studies of pneumonia, COPD and total respiratory illnesses for elderly (>65 years) (Schwartz 1994a,b,c,1995,1996; Moolgavkar et al., 1997), RR=1.19 (95% CI 1.12-1.26);

(4) APHEA European studies (Anderson et al., 1997), RR=1.114 (95% CI 1.043-1.184).

For ozone effects from multi-pollutant models, a meta-analysis was conducted for this report by pooling all available data, using a random effect model. The criteria for study selection were the same as for the mortality studies, except that some populations involved the elderly only. Eight studies were included in the analysis, and the reasons for inclusion or exclusion for individual studies are indicated in Table 12.2.b. Data include all respiratory admissions, and separate disease categories (asthma, pneumonia and COPD). The weighted mean RR for respiratory hospitalizations per 100 ppb ozone (1-hour maximum) is 1.1118 (95% CI 1.073-1.151) (or 1.12% increase per 10 ppb ozone), within the same range as those obtained from single-pollutant models.

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[4] This 1999 paper by Thurston & Ito is not an original research paper, rather a review paper, presenting meta-analyses conclusions (pooled RR estimates). It is included because the majority of the studies reviewed are also reviewed in this document (including the Canadian studies) thus the meta-analysis was not repeated independently for this document. Also, Thurston & Ito, 1999 did meta-analyses from single-pollutant models, which provide a useful comparison to the multi-pollutant meta-analysis performed here.

Table 12.2b Summary of relative risk estimates for respiratory hospital admissions due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models

Location and reference	Ozone mean ppb (range)(1-h max., unless indicated)	Outcome	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion / exclusion in quantitative analysis S: Significant NS: Non-sig
Southern Ontario Bates & Sizto, '87, '89	Winter 23.34 ppb Summer 56.07 ppb	all respiratory, asthma	Significant increase in risk. Value not given.	-	**Results S** Excluded, no data from multi-variate models
NYC Buffalo Thurston et al. '92	1988 -Buffalo: 75-164 -NYC: 69-206 1989: -Buffalo: 65-128 -NYC: 53-111	all respiratory, asthma	Respiratory: NYC: 1.40% (0.60-2.20%) Buffalo: 2.50% (0.40-4.60%) Asthma: NYC: 1.67% (0.95-2.41%) Buffalo: 3.26% (1.91-4.61%)	-	**Results S** Excluded, no data from multi-variate models
Montreal, Quebec Delfino et al., 1994.	1-h max.: May-Oct. 36 (90th: 59.2); July-Aug.: 41 (90th: 65.8). Ozone 8-h max.: May-Oct. 30.4 (90th: 51.5); July-Aug.: 35 (90th: 57.3)	all respiratory admissions Asthma admissions	1-h max. ozone: not given. 8-h avg. ozone, all respiratory: 0.41% (0.073-0.737%) + temperature. 0.676% (0.416-0.936%), no temperature.	Asthma: 1-h max. ozone: 0.175% (-0.02% to 0.37%), + PM_{10} Non-asthma respiratory: 1.65% (-22.0% to 25.3%), +sulphate.	**Results S** Included
Toronto Thurston et al. '94a,b	Mean 57.5 ppb (3 years) 2 days > 120 ppb 22 days > 80 ppb	all respiratory	3.83% (2.40-5.26%)	3.64% (2.16-5.12%), + H^{+} 3.68% (2.18-5.18%), +sulphate 2.93% (1.24-4.62%) ,+fine particles 2.81% (1.06-4.56%), +PM_{10} 2.61% (0.96-4.26%), +TSP	**Results S** Included, used data from ozone + fine particles
Minneapolis Schwartz '94c	24-h avg.: 26 ppb (10-90% 11-41 ppb)	Pneumonia in elderly	24-h ozone: 3.8% (0.4-8.0%)	24-h avg. ozone: 4.4% (0.4-9.4%), +temperatury, PM_{10}	**Results S** Included
Detroit Schwartz '94b	24-h avg.: 21 ppb (10-90% 7-36 ppb) 1-h max.: 53 ppb	Pneumonia and COPD in elderly	-	24-h avg. ozone: Pneumonia: 5.2% (2.6-8.0%), +PM_{10}. COPD: 5.6% (1.8-9.8%), + PM_{10} No data for 1-h. max. ozone	**Results S** Included

Table 12.2b Summary of relative risk estimates for respiratory hospital admissions due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models

Location and reference	**Ozone mean ppb (range)(1-h max., unless indicated)**	**Outcome**	**Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models**	**% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models**	**Inclusion / exclusion in quantitative analysis** **S: Significant** **NS: Non-sig**
Birmingham, AL Schwartz '94a	O_3 24-h avg.: 25 ppb (10-90% 14-25 ppb).	Pneumonia and COPD in elderly	24-h average ozone: Pneumonia: 2.8% (-1.2% to 7.6%) COPD: 3.4% (-2.8% to 12.0%) 1-h max. ozone: pneumonia: 0.8% (-0.6% to 2.4%) COPD: 1.4% (-0.8% to 4.0%)	-	**Results NS** Excluded, no data from multi-variate models
Southern Ontario Burnett et al., 1994	May-Aug: 52 ppb (62-118) Other months: <40 ppb.	All respiratory	May to Aug.: 0.93% (0.75-1.11%)	May to Aug.: 0.92% ($p<0.0001$), + sulphate + temperature	**Results S** Excluded, no data on variances or confidence intervals.
New Haven, Conn. Tacoma, Wa. Schwartz '95	April to Oct. 24-h avg.: New Haven : 28.6 ppb (10-90%, 15.8-45.4 ppb). Tacoma: 24.5 ppb (10-90% 13.3-35.7 ppb).	all respiratory elderly (>65 y)	24-h average ozone: New Haven: 2.35% (-0.39 to 5.10%) Tacoma: 8.23% (2.35-14.9%)	24-h avg. ozone: New Haven: 2.74% (0-5.88%), +PM_{10}, 1.96% (-0.78% to 5.1%), + SO_2 Tacoma: 7.84% (2.35-14.5%) +PM_{10} 8.24% (2.35-14.5%), + SO_2.	**Results S** Included for both cities
London UK Ponce de Leon et al. '96	O_3 8-h mean: Whole year: 15.6 ppb (10-90% 3-29 ppb); summer 7-36 ppb. O_3 1-h max: 20.6 ppb (5-95% 2-46 ppb)	All respiratory	8-h average ozone, summer: 1.66% (0.85-2.50%), all age 1.01% (-0.24 to 2.32%), 0-14 y 2.59% (1.22-4.01%), 15-64 y 2.12% (0.84-3.45%), >65 y 8-h avg., whole year: 1.13% (1.43-1.83%), all age 1.03% (-0.02% to 2.12%), 0-14 y 2.06% (0.89-3.26%), 15-64 y 1.75% (0.66-2.87%), >65 y 1-h max. ozone: 0.84% (0.56-1.12%)	Whole year ozone (8-h avg.): 1.12% (0.77-1.47%), +NO_2 1.12% (0.77-1.44%), + BS 1.10% (0.75-1.45%), +SO_2	**Results S** Included

Table 12.2b Summary of relative risk estimates for respiratory hospital admissions due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models

Location and reference	**Ozone mean ppb (range)(1-h max., unless indicated)**	**Outcome**	**Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models**	**% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models**	**Inclusion / exclusion in quantitative analysis** **S: Significant** **NS: Non-sig**
Amsterdam, Rotterdam, the Netherland. Schouten et al. '96	O_3 8-h avg.: May-Oct. (5-95%): A: 44.1 ppb (14.3-77.6); R: 42 ppb (12.8-81.1) whole year: A: 35.2 ppb (2.55-68.4 ppb); R: 32.6 ppb (3.1-71.4). O_3 1-h max.: May-Oct.: A: 49.7 ppb (21.4-88.3); R: 49.2 ppb (18.4-94.9). Whole year: A: 40.3 ppb (5.1-77.0); R: 38.8 ppb (5.6- 83.7)	All respiratory	1-h max. ozone, summer: A: 2.14% (-0.25% to 4.84%), >65 y -12.2% (-2.4% to 1.7%), 15-64 y R: 6.78% (2.6-11.7%), >65 y 0.51% (-1.2% to 2.4%), 15-64 y 1-h max., ozone, whole year: A: 1.39% (-0.45% to 3.4%), >65 y -0.02% (-1.8% to 1.9%), 15-64 y R:5.3% (1.7-9.5%), >65 y 0.86% (-1.0% to 2.96%), 15-64 y. 8-h avg. ozone, whole year: A: 1.18% (-0.8% to 3.4%), >65 y 0.02% (-1.9% to 2.18%), 15-64y R: 4.9% (0.76-9.9%), >65 y 0.04% (-2.2% to 2.4%), 15-64 y	-	**Results S** Excluded, no data from multi-variate models
Spokane, WA. Schwartz, 1996	1-h max.: 40.3 ppb (10-90% 29.6-55.6 ppb). 24-h avg.: 28.6 ppb (10-90% 20.4-37.2 ppb)	All respiratory admissions, pneumonia, and COPD, Elderly (>65 y)	all respiratory admissions: -1-h max. ozone: 9.8% (0.8-21.8%) -1-h max. ozone + tem.: 14.9% (3.5-29.4%) -24-h avg. ozone: 11.4% (-2.9% to 31.1%) Pneumonia: -1-h max. ozone: 11.6% (-2.1% to 29.1%) COPD: -1-h max. ozone: 4.9% (-9.2% to 25.7%)	-	**Results S** Excluded, no data from multi-variate models

Table 12.2b Summary of relative risk estimates for respiratory hospital admissions due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models

Location and reference	Ozone mean ppb (range)(1-h max., unless indicated)	Outcome	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion / exclusion in quantitative analysis S: Significant NS: Non-sig
Minneapolis-St. Paul, MN Birmingham, AL. 1986-1991 Moolgavkar et al. (1997)	24-h ozone: mean (10th to 90th percentile): Minn: 26.2 ppb (13.5-40.1 ppb) Birm: 25.1 (13.5-37.6 ppb)	All respiratory Pneumonia COPD Elderly (≥65 y)	Total respiratory admission: Minn: 4% (2.2-5.8%). Birm: 0.18% (–0.13% to 0.49%)	Total respiratory admission: Minn: 3.43% (1.57-5.29%) Birm: 0.18% (–0.13% to 0.49%) Pneumonia: Minn: 4.4% (2.3-6.5%) COPD: Minn: 3.0% (-0.33% to 6.3%)	**Results S** Included for both cities
Six European cities Anderson et al. 1997	O_3 1-h mean all year: A: 39.5 ppb B: 32.8 ppb L: 19.5 ppb M: - P: 18.5 ppb R: 36.4 ppb 8-h avg. all year: A: 35.2 ppb B: 28.6 ppb L: 14.3 ppb M: - P: 10.2 ppb Rotterdam: 31.1 ppb	COPD, all age	8-h avg. ozone, whole year: lag 1 d: 1.69% (0.86-2.55%) 5 cumulative days: 2.2% (1.06-3.37%) 1-h max. ozone, whole year: lag 1 d: 1.14% (0.43-1.84%) 5 cumulative days: 1.92% (0.94-2.94%) 8-h avg. ozone: cool: 1.18% (0-2.74%) warm: 1.57% (0.78-2.74%) 1-h max. ozone: cool: 0.39% (-0.78% to 1.96%) Warm: 1.18% (0.39-1.96%)	-	**Results S** Excluded, no data from multi-variate models
16 Canadian cities Burnett et al. 1997a	Spring 40 ppb Summer 38 ppb Fall 21 ppb Winter 26 ppb Whole year 31 ppb (95th percentile 60 ppb)	All respiratory	All age: Winter: -0.2% (-1.2% to 0.83%); Spring: 1.4% (0.4-2.4%); Summer: 1.7% (0.87-2.47%); Fall: 0.93% (-0.07% to 1.97%) April - Dec.: 1.40% (1.14-1.66%) <65y, 1.5% (0.7-2.3%), April-Dec. >65y, 1.3% (0.33-2.4%), April-Dec.	April - Dec.: 1.43% (1.12-1.75%), +CO 1.03% (0.70-1.40%), +CO, dew point temperature 0.80% (p=0.0258), +CO, dew point temperature, PM (soiling index), in 11 cities with available PM data.	**Results S** Included
Toronto, Ont. Burnett et al., 1997b	Daily 1-h max. 41.2 ppb (5th-95th percentile 22-69 ppb) used 3 day average for regressions	Total respiratory Cardiac admissions	3-d avg. ozone: non temperature: respiratory: 5.9% (4.0-7.8%) cardiac: 5.0% (2.2-7.8%) + temperature and dew point temperature: respiratory:5.6% (3.5-7.7%) cardiac: 6.4% (3.1-9.6%)	-	**Results S** Excluded, no data from multi-variate models

Table 12.2b Summary of relative risk estimates for respiratory hospital admissions due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models

Location and reference	Ozone mean ppb (range)(1-h max., unless indicated)	Outcome	Percent increase (95% CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Ozone only models	% increase (95%CI) per 10 ppb ozone (1-h max., unless indicated otherwise). Multi-pollutant models	Inclusion / exclusion in quantitative analysis S: Significant NS: Non-sig
10 Canadian cities Burnett et al., 1997c	Daily 1-h max.: 32 ppb (5th –95th percentile: 10-64 ppb) 24-h avg.: 16 ppb (5th-95th percentile 3-35 ppb)	Congestive heart failure in elderly (>65 y)	24-h avg. ozone: not controlled for temperature 0.30% (0.03-0.57%) + temperature and dew point temperature: 0.32% (-0.025% to 0.66%)	+ temperature, DP temperature, CoH, NO_2, SO_2, and CO: 0.30% (0.006-0.594%)	Excluded, no respiratory data
Canada Burnett, 1998	O_3 1-h max: 31 ppb Range: (25-38 ppb)	All respiratory	1.04% (0.78-1.30%)	-	Excluded, no data from multi-variate models
Meta-analysis	Meta-analysis of multi-pollutant analyses, weighted mean increase (%) in respiratory hospitalizations +/- SD = 1.12% +/- 0.20% (n=8) per 10 ppb increase in ozone (1-hr max), 95% CI: 1.073 - 1.51%, $p<0.05$. Meta-analysis of single-pollutant analyses (Thurston and Ito, 1999), weighted mean increase (%) in respiratory hospitalizations +/- SD = 1.8% +/- 0.41% (n = 6) per 10 ppb increase in ozone (1-hr max), 95% CI: 1.0 - 2.6%, $p<0.05$.				

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12.4 MORBIDITY—ACUTE EFFECTS: EMERGENCY DEPARTMENT VISITS

As with hospitalizations, emergency department (ED) visits provide a relatively objective and measurable indicator of the impact of ambient ozone concentrations on public health, by making use of administrative data records. A greater element of subjectivity than with hospitalizations is included in emergency department visits, since a visit is usually the result of an individual's (or family's) own decision that health has been seriously impaired, and that medical attention should be sought immediately. Partly because of this element of individual choice and partly because the health impact is not as severe, on average, as with individuals who have been hospitalized (by doctor's orders), the ED visit rates should be (and are) much higher than the hospitalization rates, thus demonstrating the applicability of the 'pyramid of effects' as set out by the American Thoracic Society (1985). Some idea of the relationship between hospitalizations and ED visits can be obtained from the study by Stieb et al. (1995a), who administered a questionnaire to a sample of 52 asthmatic volunteers in Winnipeg. One-quarter had visited an emergency department in the previous year for respiratory illnesses, while five percent (not necessarily the same individuals) had been hospitalized in the same period, a ratio of one hospitalization to every five ED visits. A similar set of results (a mean of 0.6 hospitalizations versus 2.7 ED visits in the past 12 months) was observed in Saint John, N.B. for ED patients discharged with asthma, in response to a questionnaire (Stieb et al., 1995b).

Ten studies utilizing emergency department visits as the outcome, were reviewed as an extension to the hospitalization series of studies, using the same criteria against which to judge the scientific merits and the reliability of the information on associations with ozone which they provided. These studies are presented in Table 12.3. Three of these studies were included in the combined analysis of hospitalizations and ED visits in the recent U.S. EPA Criteria Document on Ozone (1993). Two studies included in the EPA analysis were not included here (Tseng et al., 1992; Sunyer et al., 1991), since their methodology was judged (by the EPA reviewer) to be inappropriate and/or inadequate for detection of an ozone effect.

12.4.1 Studies reporting significant positive associations between ozone and Emergency Department visits

Six of the ten studies reviewed in this document found statistically significant associations between ozone levels and ED visits for asthma or for all respiratory causes (Cody et al., 1992; Weisel et al., 1995; White et al., 1994; Romieu et al., 1995; Delfino et al., 1997; Jones et al., 1995). The authors of the studies used various analytical techniques to detrend the ED visits and ozone data, and were successful in adjusting for the effect of temperature, a known confounder with ozone, by inclusion into the regression equation. Table 12.3a gives an overview of methodology and results of the individual studies, and Table 12.3b presents a summary of ozone risks associated with increased ED visits for respiratory diseases.

Risk of increased ED visits

The percent increase in ED visits from these studies varies from 6% to 8.6% per 10 ppb of 1-hour maximum ozone (Romieu et al., 1995; Delfino et al., 1997), or 5.6% to 14.2% per 10 ppb of 5-hour or 8-hour average ozone (Cody et al., 1992; Weisel et al., 1995, Delfino et al., 1997), or 11% per 10 ppb of 24-hour average ozone (Jones et al., 1995). Most studies controlled for seasonal and temperature variations. Three studies controlled for SO_2 (Cody et al., 1992, Weisel et al., 1995, Romieu et al., 1995), and three studies controlled for PM (Weisel et al., 1995, White et al., 1994, Delfino et al., 1997). The adjustment for environmental factors did not substantially reduce the risk of ozone-associated respiratory ED visits. As expected, the impact of ozone on respiratory ED visits is higher than on mortality (0.4% increase per 10 ppb) and hospitalizations (1.12% per 10 ppb). The results are considered consistent for the ED studies, given that two studies looked at children, two were for all ages in general, and two for 3 or 4 individual age groups.

Concentrations at which adverse outcomes were observed

The ED results were obtained from four cities or areas (Montreal, Quebec; central New Jersey adjacent to New York City; Atlanta, Georgia; and Mexico City), in three countries, representing a wide range of average ozone concentrations, between 30 and 90 ppb for the high summer season. Montreal had the lowest ozone concentrations at 33.2 and 36.2 ppb (mean of 1-h daily maximum) for 1992 and 1993 respectively, and the ozone value never exceeded 79 ppb (82 ppb is the Canadian objective). In Montreal, in line with the low ozone levels, the association with ED visits was not significant for ozone in 1992, but was significant in 1993. Mexico City had the highest average ozone levels, at a mean (1-h max.) of 90 ± 40 ppb, with 28% of days above 110 ppb (the Mexican objective).

Age of respondents

In Montreal (Delfino et al., 1997), only the elderly were significantly impacted by ozone, of the four age groups examined (< 2 years, 2-34 years, 35-64 years, 65+ years). This is not necessarily inconsistent with other studies in which children were found to be affected by ozone, because in the Delfino study, all respiratory diagnoses were included rather than asthma alone, due to a lack of diagnostic specificity in the database to separate out asthma. In Jones et al., (1995) the ozone effect on the elderly respiratory ED visits was marginal ($p<0.11$) compared with people aged 18-60 years ($p<0.04$). The elderly are more likely than younger age groups to have COPD or other conditions that compromise lung function, and are less likely to suffer from asthma. Two studies examined asthma visits in children (<16 years) (White et al., 1994; Romieu et al., 1995). Both studies found a significant association between ozone (1-hour maximum or 5-hour average) and children's asthma ED visits, after adjusting for temperature, and/or SO_2.

Concentration-response relationships.

Three of the studies reporting statistically significant results looked at the dose-response relationships by dichotomizing or categorizing their data on ozone levels, in addition to the regression analysis on continuous data. Weisel et al. (1995) found that for days with ozone > 60 ppb (average of 5 h from 10 am - 3 pm), there were 25.5% more visits by all age groups for asthma-related conditions than for days with ozone <60 ppb (p=0.0029).

For children in Atlanta GA (White et al., 1994), 43% more ED visits (95% CI 4-97%) were recorded for days when ozone (1-h maximum) was higher than 110 ppb compared to the days with ozone below 110 ppb. White et al. (1994) also examined the concentration-response relationship at ozone levels from 80 ppb to 110 ppb. RR for ozone-associated asthma visits increased monotonically from 1.01 (at 80 ppb) to 1.5 (110 ppb), although the RR was statistically significant at 110 ppb only.

In the study of Mexico City children (Romieu et al., 1995), 68% more asthma-related ED visits (95% CI 30-171%) were recorded on occasions when preceding and concurrent two days were above 110 ppb (mean of daily 1-h maximum). When ozone levels (1-hour maximum) during two preceding days were above 110 ppb, asthma-related ED visits increased 133% (95% CI 83-196%) (Romieu et al., 1995).

Table 12.3a Ambient ozone and emergency department visits

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Cody et al. 1992 central New Jersey 9 hospitals May –Aug. 1988-89 (2 summers)	ED visits, asthma and bronchitis, all ages; mean 28.7 y (1988), 29.9 y (1989) mean visits 3.6/d- asthma, 4.0/d- bronchitis, 18.0/d – wounds Total: : asthma 814; bronchitis 912; wounds 4066	O_3 -10 am-3pm (5 h means): 0.55 ppm (1988) 0.043 pp (1989) 34 days >120 ppb (1988) 8 days > 120 ppb (1989) 5 monitoring sites ((R=0.58-0.88 between sites)	SO_2- 9 ppb mean PM_2 (every 6th day) (no values given) visibility as surrogate for SO_4 also monitored temperature, pressure, relative humidity, 5 monitoring sites (3 near hospitals)	OLS multiple regression -Temp highly correlated with ozone, (r=0.64) therefore included in regression -lag days 0, 1, 2 checked -anal. Incl. SO_2, RH, visibility, -PM_{10} incl., separate model. -autocorrelation check	-Bivariate models: ED visits for asthma correlated with temperature (r^2=0.052, p=0.0006), and with ozone (r^2= 0.025, p=0.0147). indicating confounding effects of temperature. -Multivariate analysis of all environmental variables (SO_2, temperature, RH, visibility) and asthma visits, only ozone and temperature showed contribution: O_3 (5-h avg.), coefficient with asthma (SE, p), (% increase per 10 ppb, SE): 1988-1989 (lag 1d): 20.3 (7.17, p=0.005), (5.6%, 2.0%) 1988 (lag 1d):24.6 (8.28, p=0.0041), (7.4%, 2.5%) 1989 (lag 0d): 37.2 (13.5, p=0.0067), (9.7%, 3.3%); (lag 1d) 27.7 (11.8, p=0.0206), (7.3%, 3.0%). -Concluded 7%-9% increase in asthma visits was contributed to ozone (48 ppb mean); then for each 10 ppb, it was 1.4% to 1.9%. -No environmental associations seen with bronchitis or control cases (finger cuts). -correlation not significant for PM_{10} -1 day in 6 for particles, + visibility as surrogate for SO_4 may be inadequate, Therefore part of effect ascribed to ozone could have been from these -Checked for day of week effects, but not found important -did not control for seasonality, but used ozone season data only. -did not consider NO_2, SO_4, H^+
Weisel et al. 1995 central New Jersey May- Aug. 1986-90 (5 summers)	ED visits, asthma mean visits 5.36/day, range 4.49-6.05 (5 years)	O_3 52.8 ppb (5-y mean, 10 am-3 pm) range 46 - 57 ppb (5 years) Monitoring as in Cody et al. 1992	SO_4 , NO_2 , SO_2, visibility monitored but values not given -temp., relative humidity, rate of temp. change also recorded -PM_{10} not mentioned, but monitored in previous study, and possibly in this. Monitoring as in Cody et	-daily ED visits for asthma, all ages -looked at different lag times, considered visits from 3pm to 9 am, same day and lag 1 day -OLS multiple regression -Temperature, rate of temperature change, and relative humidity considered in prelim. Anal, but only ozone and temp. incorporated into	-Multiple regressions, controlled temperature, RH, sulphate, NO_2, SO_2, visibility, ED visits correlated with O_3 significantly. % increase asthma ED visits (SE) per 10 ppb: 1986: 7.1% (3.6%) 1987: 7.7% (3.0%) 1988: 7.0% (3.0%) 1989: 14.2% (3.2%) 1990: 6.9% (2.5%) -temperature explained 7.6% to 34% of variability (1988 lowest, 1990 highest)

Table 12.3a Ambient ozone and emergency department visits

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
			al. 1992	regression. -Ozone values were lagged 24, 48 hours for regression, each year regressed separately -covariance anal. For 60 ppb cutoff point, adj. For temp. -autocorrelation considered	-Low (<60 ppb) vs. high ozone (≥60 ppb), 5-year data: 25.5% increase in asthma visits due to ozone, $P<0.0001$. -When adjusted for temperature, ozone mean effect 3% per 10 ppb. -Daily SO_4, NO_2 visibility, and every 6th day SO_2 not correlated to ED visits. -analysis successfully decoupled temperature (most important potential confounder) from effects of ozone on ED visits.
White et al. 1994 Atlanta, GA (2 counties, 1 hospital in low soc.-econom. status area, 55,000 mostly black children, within 6 mi. of 1 hospital, 3 mo., , June-Aug 1990	ED visits, asthma in children, ages 1-16 (infants excluded) 609 visits in 92 days, (6.6± 3.06 visits/day) average age 6y	O_3 1-h max: 78ppb (range 15-163 ppb) 8-h mean: range 13-125 ppb (mean not given) O_3 > 110 ppb for 6 of 92 days 2 monitors, 1 and 7 miles from hospital correl. High(R=0.87)	SO_2 17-139 ppb PM_{10} 39.4 ug/m^3 (24-h mean) 67 ug/m^3 (mean of 1-h max.) dewpoint , temperature. and pollen counts also measured PM_{10} monitors in state network, + 1 of 2 O_3 monitoring locs, for 6 weeks (1/2 of time)	-daily ED visits for asthma, mostly black children, from low SES area -excl. bronchiolitis, pneumonia, + repeat visitors Poisson regression; included temp., day of week, PM_{10} (lag1); checked various time lags, autoregression 2nd Poisson regr. with generalized estimating equation for serial correlation	-Single pollutant model, not control of temperature, for asthma visits: 1-h max. ozone: >110 ppb RR=1.33, 95% CI 0.94-1.71 8-h avg. ozone, number of asthma visits: <80 ppb, 6.53 (5.83-7.23); >80 ppb, 6.61 (5.14-8.08); <90 ppb, 6.43 (5.79-7.07); >90 ppb, 8.00 (4.89-11.1). -RR (95% CI) for 110 ppb or high ozone (1-h max.) for other causes of visits: Total visits: 1.37 (1.02-1.73) Non-upper respiratory infection: 1.53 (1.14-1.92). -Multivariate analysis: • controlled for temperature, PM_{10}, day of the week: RR for asthma visits at ozone >110 ppb (1-h max.): 1.42 (0.99-2.0, p=0.057). • also corrected for autocorrelation + above factors, RR=1.43 (1.04-1.97) • controlled for temperature, PM_{10}, day of the week, pollen: RR=1.33 (0.91-1.92). • controlled for temperature, PM_{10}, day of the week, dose-response relations: 80-90 ppb, RR=1.01 (0.75-1.36); 90-99 ppb, RR=1.24 (0.93-1.65); 100-109 ppb; RR=1.29 (0.86-1.93); 110 ppb, RR=1.50 (1.02-2.21). - PM_{10} RR=1.02 for a 10 ug/m^3 incr. (CI 0.96-1.13; n.s.) -Seasonality was reduced by the study period selection, but within the season cycles not addressed.

Table 12.3a Ambient ozone and emergency department visits

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
Romieu et al. 1995 Mexico City, north- central area, low SES, 1 pediatric hospital (serves approx. 450,000 children) Jan-June 1990, (dry season Nov.-May, with highest air pollution)	ED visits, asthma (ICD-9 code 493), other respiratory diseases (IDC-9 codes 460-464, 466, 480-486), and non-respiratory diseases Children<16 y, 1 pediatric hospital serving approx 450,000 children Asthma visits 2.14/day (total 395) Respiratory visits 7.58/d (total 1365) Total visits, incl. non-respiratory, 15,698	mean O_3 1-h max 90 ±40 ppb (range 10-250) O_3 >110 ppb on 28% f days (49 d) Also O_3 8-h moving average Air monitoring station located in residential catchment area of hospital	Mean SO_2 70 ppb Mean NO_2 30 ppb Mean TSP 474 ug/m^3 (range 238-672) Measurements included daily min. temp., NO_2 and SO_2 24-h mean, SO_2 daily 1-h max., O_3 daily 1-h max and 8-h moving average. - TSP (by hi-vol sampler) was measured only every 6 days, total 44 days during the study period. -Air monitoring station located in residential catchment area of hospital	Poisson regression model. Terms for day-of-week effects, seasonal effects (Jan-Mar vs. Apr.-Jun) included. Three different lag times included (lag 0-lag 2). Two age categories examined (< 5 years, ≥ 5 years) -children < 5 y suggested as sl. more susceptible to effects of ozone	-50 ppb incr. in 1-h max. O_3 (lag 1d) assoc. with 43% incr. in asthma visits (RR=1.43; 95% CI 1.24-1.66, after accounted for potential confounding of day of the week, period, SO_2, temperauture). 50 ppb incr. in 1-h max. O_3 (lag 1d) assoc. with 43% incr. in asthma visits (RR=1.43; 95% CI 1.23-1.65, after accounted for potential confounding of day of the week, period, SO_2, temperauture, sex, age). -2 consecutive days (preceding and concurrent days) with O_3 >110 ppb gave 68% incr. in ED asthma visits (RR1.68, 95%CI 1.30-2.71). -RR=2.33 (95% CI 1.83-2.96), 133% increase, after high ozone levels on the 2 preceding days before the asthma-related ED visits. -O_3 also correl., (but weaker) with other resp. visits (P=0.02, 0.06 for lags 0,1) - SO_2, a 50 ppb increase in same day 1-h max., was marginally assoc. with a 5% increase in ED visits for asthma (RR 1.05; CI 0.99-1.11), and was strongly associated with other respiratory visits (p=0.002) - Exposure to particulate matter was not a significant predictor of asthma-related visits (but only 44 days available for analysis (authors noted inability to assess PM accurately) Analysis carefully done, but basic no. of visits very small.
Castellsague et al. 1995 Barcelona, Spain 5 years, 1985-1989 (4 years for O_3, excl. 1986)	ED visits for asthma, as recorded in asthma registry (validated for reliability) Residents >14 y old, to age 65 4 hospitals, incl. 80% of asthma visits Mean asthma visits -	Ozone 1-h max, ppb (converted from ug/m^3) Summer/winter mean 43/29 75th 53/35 95th 71/53	Pollutant mean (ppb) Summer winter NO_2 54 52 95th 96 80 SO_2 15 19 95th 31 35 BS (black smoke, ug/m^3) mean 48.2 68	-Poisson regression anal. -stratified by season, winter- Jan-Mar. summer- July-Sept -time trends tested with linear and quadratic terms for long trends, indicator variables for study year, month, and day of week -weather variables included	-No associations were found between ED visits for asthma and either O_3 or SO_2 -After adjusted for temperature and RH, month, day of the week, and soybean unloading, RR= 0.991 (summer, 95%CI 0.939-1.045) and 1.055 (winter, 95% CI 0.998-1.116) for 12.8 ppb O_3, p=0.1. -SO_2 , NO_2 and BS were associated with asthma visits in summer and in winter; the association was higher for a 1-day lag. -No multi-pollutant regression were done.

Table 12.3a Ambient ozone and emergency department visits

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
	2.7/day in summer, 3.9/day in winter (Total 912 visits)			temperature (min., max, mean), RH, dew point. (not clear if considered before or in the regression) lags 0-5 days tested, also tested cumulative exposure	-No correlation coefficient between ozone and co-pollutants was given. -Ozone levels were lower in Barcelona than in other cities where positive associations have been observed. This, combined with very low asthma visits/day and higher than average NO_2 may have accounted for the nonsignificant findings.
Rennick & Jarman 1992 Melbourne, Australia 1 year, 1989	ED visits, asthma All children > 2 years old -excl. repeat attendance < 3 days apart -1 hospital	for ozone days, average 2.7 (range 1-6) stations recorded ozone levels >120 ppb (1-h) and >50 ppb (8-h avg.).	Aiboome particulate index, 5 stations (range 2-6) had API breach.	Pearson correlation analysis done on ozone and other pollutants. ANOVA used to control for confounding variables. Stepwise multiple regression analysis used for associations.	-Smog alert days not significantly related to asthma ED visits. -Ozone days not significantly related to asthma visits. Results not given. -Seasonality controlled by examining during summer and during ozone days. -No temperature controlled. -multiple stepwise regression did not reveal ozone effect. Results not given. -Significant association between asthma ED visits and API, $p<0.005$.
Delfino et al., 1997 Montreal, Canada (pop. 3,000,000) June-September 1992-1993 (2 summers) 25 hospitals	ER visits for all respiratory illness, asthma All ages separated into ages <2y, 2-18y, 19-34y, 35-64y, 65+y Mean of respiratory visits: 1923 visits; 98/d	O_3 1-h max (mean): 1992 1993 28.8ppb 30.7ppb O_3 8-h mean: 1992 1993 33.2ppb 36.2ppb 10 monitoring stations correl high: r=.80 (except for one station for which r=0.70)	Measured as a 24-h period: 1992 PM_{10}: 30.1 µg/m^3 $PM_{2.5}$: 18.5 µg/m^3 SO_4: 51.7 nmole/m^3 H^+: 11.3 nmole/m^3 1993 PM_{10}: 21.7 µg/m^3 $PM_{2.5}$: 12.2 µg/m^3 SO_4: 34.8 nmole/m^3 H^+: 4.0 nmole/m^3 Also monitored	-OLS multiple regression, using a 19-weighted linear filter to remove temporal trends and weather variables -Same day and lag days 1,2 checked -Autocorrelation check	-No significant association with ER visits were found for 1992 (33% of the particulate data were missing), data not reported. For 1993 results: -No ozone effects on age 2-64y, data not shown. -For age <2y, no ozone effect reported, presumably not significant. -For age >64 y, respiratory ED visits: - single-pollutant model: 1-h max. lag 1d ozone 10 ppb assoc. with 5.9% increase of visits (SE 1.78%); 8-h max. lag 1d ozone 10 ppb assoc. with 7.2% (SE 2.2%) increase in visits. - 8-h max. Ozone+PM2.5, 10 ppb assoc. with 5.7% (SE 2.8%) increase in visits. - When controlled for weather, single-pollutant model, ozone effect did not change

Table 12.3a Ambient ozone and emergency department visits

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
			temperature and relative humidity		effect did not change. -H^+ was significant for infants under age two (5% increase in ER visits) but was no significant for the elderly -O_3 and PM_{10} never exceeded 67 ppb and 51 µg/m^3 respectively (1993). -PM_{10} and $PM_{2.5}$ along with SO_4 were significant predictors of 16% and 12% respectively, of increases in ER visits (total respiratory) for the elderly (65+y). -1-h max. and 8-h avg. ozone were highly correlated (r=0.97). -Ozone correlated with PM_{10} (r=0.63), $PM_{2.5}$ (r=0.63), SO_4 (r=0.58), H^+ (r=0.46), and temperature (r=0.70).
Jones et al., 1995 Baton Rouge, Louisiana June 1, 1990 to August 31 1990 (92 days) 3 hospitals	Respiratory-related ED visits: (pneumonia, sinusitis, COPD, bronchitis, croup, asthma, shortness of breath and upper respiratory tract infection) 3 age categories: -pediatric (0-17y) -adults (18-60y) -geriatric (61+y)	Daily average O_3 28.2 ± 11.7 ppb (range 9.3-57.9 ppb) O_3 1-h max (mean): 69.1 ± 28.7 ppb (range 25.3-165 ppb) 4 days > 120 ppb 3 monitoring stations (r=0.95)	No other pollutants were measured Also monitored daily temperature and hourly relative humidity at 2 monitoring sites -Total respiratory-related ED: 1265 visits -Pediatric: 369/d -Adult: 629/d -Geriatric: 267/d	-Multiple regression analysis -Terms of temperature, humidity, mold, pollen counts, days of the week effects were examined -Autocorrelation check -Lag 2 days tested	-Respiratory-related ED visits in summer (June to Aug.) were significantly associated with 24-h ozone in adult (18-60 y), not assoc. with elderly (60+ y) and children (0-17y). -Single pollutant models: correlations between 24-h avg. ozone and daily respiratory ED visits were seen only in adults. Slopes (SE, t): Children: -0.028, (0.017, -1.63) (-7.0% increase per 10 ppb, 95% CI –15.4% to 1.4%) Adult: 0.076 (0.025, 2.99)(11.1% increase per 10 ppb, 95% CI 3.8-18.4%). Elderly: 0.013 (0.019, 0.70) (4.5% increase per 10 ppb, 95% CI –1.9% to 10.9%). -Multiple regressions with ozone, temperature, RH, mold and pollen, respiratory ED visits slope (t): - Children: -0.026 (t= –1.18), p<0.24, (-6.5% increase per 10 ppb, SE 5.5%, 95% CI –17.3% to 4.3%) - Adults: 0.068 (t=2.12), p<0.04, (9.9% increase per 10 ppb, SE 4.7%, 95% CI 0.71% to 19.1%) - Elderly: 0.039 (t= 1.59), p<0.11, (13.4% increase per 10 ppb, SE 8.4%, 95% CI –3.2% to 30.0%). -Day of the week do not appear for a factor in determining the respiratory-related ED visits (tested by One-way ANOVA) -44% of the adults and 43% of pediatric respiratory-related ED

Table 12.3a Ambient ozone and emergency department visits

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
					visits were due to asthma -For geriatric respiratory-related ED visits, the predominant diagnosis were COPD (28%)
Bates et al., 1990 Vancouver, Canada (pop. approx.: 1,000,000) July 1, 1984 to October 31, 1986 (3 summers) 9 hospitals	ED visits, asthma (ICD-9 code 493), other respiratory diseases (ICD-9 code 466, 480-486, 491-492 and 496) and non-respiratory diseases All ages separated into ages 0-14y, 15-60y, 61+y 25 500 visits/months where 2.7% for respiratory conditions and of these, 41.3% for asthma	O_3 mean of the daily hourly maximum for all stations: Mean for a week in summer: 30.4 ppb and in winter: 18.8 ppb 11 monitoring stations	Mean of maximal hourly values for: SO_2, NO_2 and CoH (values not given) Also monitored: daily temperature SO_4 were collected between October 84 and December 86 at 2 monitoring sites: Winter (Nov.-April): 3.15 µg/m^3 Summer (May-Oct.): 3.54 µg/m^3	-Intercorrelations between environmental variables and emergency visits (Pearson correlation) -Stratified by season: Winter: November to April Summer: May- October (coefficients were calculated on the same day and lagged 24 and 48 hr)	-1-h max. ozone moderately correlated with SO_2, NO_2, SO_4 and CoH in summer (r ranging from 0.125 with sulphate to 0.35 with NO2), and in winter (r ranging from 0.308 with NO2 to 0.56 with CoH). -O_3 is strongly related to temperature, r=0.64 in summer, r=0.57 in winter. -Simple Pearson correlation shows: - In summer ozone was associated significant with total ED visits in all age groups (1-14 y, 15-60 y, 61+), and not significantly assoc. with asthma or respiratory visits. - In winter, ozone was assoc. with total ED visits only in adult group (15-60y). - The analysis did not take into account temperature, day of the week, within the season other cyclic variations, other pollutants, etc. -No risk estimates were given. -Total ED visits also significantly positively correlated with temperature in both summer and winter. -There was a day of the week effect on respiratory visits. -Respiratory visits are not related to temperature, O_3 or , NO_2 -Asthma and respiratory visits (group 15-60y) are correlated in summer with SO_2 and SO_4 ($p<0.001$) -In the 61+y group only, respiratory visits in the winter are related to NO_2 levels on the same day, and lagged 24 and 48 hr; asthma visits were related to SO_2
Kesten et al., 1995 Toronto July 1, 1991 to June 30, 1992 (1 year)	ED visits, asthma Total ER visits for asthma: 854 visits; 2.38 visits/d (highest number of	O_3: average of hourly measurements over a 24-h period (data not given)	Measured as an 24-h basis (data not given): SO_2 NO_2 Air pollution index	-Daily, weekly and monthly averages of the number of emergency room visits for asthma -Autoregressive technique; the number of visits, which is	-No association between emergency room visits for asthma and outdoor levels of SO_2, NO_2, O_3 and overall air quality index (on a daily, weekly or monthly basis). -Visits staggered by 1 and 7 days: relationship between emergency room visits and air pollution index and air quality index -Visits staggered by 7 days: associations were found between

Table 12.3a Ambient ozone and emergency department visits

REFERENCE	ENDPOINT	MEAN O3, PPB	OTHER POLLUTANTS	STUDY DESIGN	RESULTS AND COMMENTS
one hospital (Toronto hospital)	visits is occurring in May and between September and December)		Air quality index Also monitored: daily temperature	the dependent variable, was fitted using the AUTOREG procedure from SAS, version 6.04	asthma ED visits and NO_2 (p=0.005), and O_3 (p=0.035). -Visits staggered by 1 day: no associations were found between asthma ED visits and NO_2 and O_3. -No detailed value of risk was given in the text. -Did not mention on the adjustments for season, weather, other pollutants, etc., likely did not control for these environmental factors.

Table 12.3b Summary of relative risk estimates for Emergency Department Visits due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models

Location and reference	Ozone mean oncentrations and range	Outcome (population included)	Percent increase (95% CI) per 10 ppb ozone. Ozone only models.	Percent increase (95% CI)_ per 10 ppb ozone. Multi-variate models.
New Jersey, USA Cody et al. 1992	49 ppb (mean of 5 h from 10am-3pm) 34 days >120 ppb (1988) 8 days >120 ppb (1989)	asthma, bronchitis (all ages)	-	5-h avg. ozone: +SO_2, temperature, RH, visibility: 1988-1989 (lag 1d): 5.6% (1.7-9.5%); 1988 (lag 1d): 7.4% (2.5-12.3%); 1989 (lag 0d): 9.7% (3.2-16.2%); 1989 (lag 1d): 7.3% (1.4-13.2%)
New Jersey, USA Weisel et al. 1995	53 ppb (mean of 5 h from 10am-3pm)	asthma (all ages)	-	5-h avg. ozone: +temperature, RH, sulphate, NO_2, SO_2, visibility: 1986: 7.1% (0.04-14.2%) 1987: 7.7% (1.8-13.6%) 1988: 7.0% (1.1-12.9%) 1989: 14.2% (7.9-20.5%) 1990: 6.9% (2-11.8%)
Atlanta, Ga., USA White et al. 1994	78 ppb (mean of 1-h daily max.) (range 10-163 ppb)	asthma (children, ages 1-16 yr., mostly black, low SES)	1-h max. ozone, when >110 ppb for asthma visits: 33% (-6% to 71%) for other causes of visits: Total: 37% (2-73%) Non-upper respiratory infection: 53% (14-92%).	1-h max. ozone: + temperature, PM_{10}, day of the week: asthma visits at ozone >110 ppb: 42% (-1% to 100%, p=0.057). also corrected for autocorrelation + above factors: 43% (4-97%) + temperature, PM_{10}, day of the week, pollen: 33% (-9% to 92%). +temperature, PM_{10}, day of the week, dose-response relations: 80-90 ppb, 1% (-25% to 36%); 90-99 ppb, 24% (-7% to 65%); 100-109 ppb; 29% (-14% to 93%); 110 ppb, 50% (2-121%).
Mexico City, Mex. Romieu et al. 1995	90 ±40 ppb (mean of 1-h daily max) (range 10-250 ppb) (28% of days >110 ppb)	asthma (children, <16 y)	-	1-h max. ozone: 8.60% (4.8-13.2%) +temperature, SO_2, day of the week; 8.6% (4.6-13.0%) +temperature, SO_2, day of the week, sex, age
Vancouver, BC Bates et al., 1990	1-h max., 30.4 ppb in summer; 18.8 in winter	Asthma, other respiratory and non-respiratory visits. All age, & 0-14 y, 15-60 y, 61+y	1-h max. ozone: Associated with total ED visits; not with respiratory visits. No values given.	-
Barcelona, Spain Castellsagne et al., 1995	1-h summer: 43 ppb, winter: 29 ppb	Asthma, 14-64 y.	1-h max. ozone: No association Value not given.	1-h max. ozone: +Temperature, RH, month, day of the week, soybean loading: Summer: -0.7% (-4.7% to 3.5%). Winter: 4.3% (-0.16% to 9.1%).
Melbourn,	For ozone days,	Asthma, >2 y	-Smog alert days not significantly	-

Table 12.3b Summary of relative risk estimates for Emergency Department Visits due to a 10 ppb increase in ozone concentrations, in univariate and multi-variate models

Location and reference	Ozone mean oncentrations and range	Outcome (population included)	Percent increase (95% CI) per 10 ppb ozone. Ozone only models.	Percent increase (95% CI)_ per 10 ppb ozone. Multi-variate models.
Australia Rennick & Jarman, 1992	average 2.7 (range 1-6) stations recorded ozone levels >120 ppb (1-h) and >50 ppb (8-h avg.).	children	related to asthma ED visits. -Ozone days not significantly related to asthma visits. Results not given.	
Toronto, ON Kesten et al., 1995	Data not shown	Asthma visits for all ages.	-Asthma visits not assoc. with ozone on daily, weekly or monthly basis; -associated with ozone with 7 day lag, but not 1 day lag. No value given	-
Montreal, Quebec Delfino et al. 1997	8-h: 1992: 33 ppb; 1993: 36 ppb; 1-h: 1992: 29 ppb; 1993: 31 ppb	all respiratory, asthma (all ages, separated into ages <2y, 2-34y, 35-64y, 65+y)	-No assoc. in 1992, no value given. -1993, no assoc. in <2y and 2-64y, no value given -1993, significant associations in >64y. 1-h max. ozone: 5.9% (2.4-9.4%); 8-h avg. ozone: 7.2% (2.9-11.5%).	1993 data, 8-h avg. ozone: the Elderly: 5.7% (0.21-11.2%) +PM2.5
Baton Rouge, Louisiana Jones et al., 1995	69.1 ppb (mean of 1-h max) (range 25.3-165 ppb) 4 days >120 ppb. 24-h average 28.2 (9.3-57.9).	all respiratory (all ages, separated into ages 0-17 y, 18-60y, 61+y	24-h avg. ozone: Children: -7.0% (–15.4% to 1.4%) Adult: 11.1% (3.8-18.4%). Elderly: 4.5% (–1.9% to 10.9%).	24-h avg. ozone, +temperature, RH, mold, pollen: Children: -6.5% (-17.3% to 4.3%) Adults: 9.9% (0.71-19.1%) Elderly: 13.4% (–3.2% to 30.0%).

Confounding effects of seasonal and weather variations

The variations in season and weather are known often to have close correlations with ozone and health outcomes, and may confound the results. All the studies reporting significant associations tried to control long wave seasonal variations of ozone and ED visits either by filtering techniques (Delfino et al., 1997), or by limiting studies to ozone season only (Cody et al., 1992, Weisel et al., 1995, White et al., 1994, Romieu et al., 1995, Jones et al., 1995). There is a limitation for the latter methodology, since using one-season data still cannot eliminate the within season cyclic variations.

All the studies attempted to adjust for the effects of temperature, many of which conducted co-regression with temperature as a co-variate. The adjustment for temperature did not substantially reduce the ozone effects, and ozone continued to be associated with respiratory ED visits.

Co-occurring pollutants

With respect to other air pollutant covariates, PM should also have been correlated with emergency department (ED) visits, based on other studies not examined in detail for this review. Direct measures of PM_{10} and $PM_{2.5}$ were available for the Montreal study (Delfino et al., 1997). Particles, along with sulphate, were significant predictors of increases in ED visits (total respiratory) for the elderly (> 64 years of age) 16% and 12% respectively (Delfino et al., 1997). By comparison, a stronger association was observed for ozone at 21% of increases in ED visits (for a 36 ppb increase in mean ozone). The predicted increase due to sulphate was only marginally significant at 6%. Particle strong acidity, as H^+, was also directly measured in this study, and was significant for infants under age two (5% increase in ED visits including a lag of 2 days and relative humidity in the model), but was not significant for the elderly or any other age groups (Delfino et al., 1997). Because of the potential confounding effects of PM on ozone-ED visit associations, PM_{10} was co-regressed with ozone in this study. After the adjustment of PM_{10}, ozone remained significantly associated with respiratory visits [6% increase in ED visits per 10 ppb ozone (8-hour average), SE 2.8%].

Although daily PM_{10} measurements were available for just under half the duration of the Atlanta children study (White et al., 1994), the authors conducted regressions with PM_{10} and ED visits. The association of PM_{10} with ED visits was positive, but was non-significant. Co-regression with PM_{10} did not reduce the effect of ozone on children's asthma ED visits (White et al., 1994).

Mean particulate levels (as TSP) were very high in Mexico City, at a mean of 474 $\mu g/m^3$, but did not show significant association with respiratory ED visits (Romieu et al., 1995). One explanation for the non-significance may have been related to the fact that only 44 days of measurements were available due to the 6-day monitoring schedule. The authors noted that the effect of particulate matter could not accurately be assessed from their data. TSP was not highly correlated to ozone levels (r=0.25) (Romieu et al., 1995), and was not adjusted for during the analyses.

Cody et al. (1992) used visibility as a surrogate for PM. Results of co-regression of visibility with ozone showed that ozone was significantly associated with all-age asthma ED visits. Weisel et al. (1995) used sulphate to represent PM effects, and found no significant confounding effect on the ozone-asthma relationship. The association in this study was consistent in all five years examined (1986-1990). Sulphate was not found to be correlated with asthma-ED visits (Weisel et al., 1995).

Three studies investigated the potential effect of SO_2 (Cody et al., 1992, Weisel et al., Romieu et al., 1995), and one study examined the effect of NO_2 (Weisel et al., 1995). After the adjustment of SO_2 or NO_2, ozone maintained its significant association with respiratory ED visits. Pollen and mould also did not seem to confound the ozone effect on respiratory ED visits (Jones et al., 1995). Co-regressed with pollen, mould, temperature and relative humidity, ozone was still revealed to be significantly associated with respiratory ED visits (slope= 0.068/ppb, $p<0.04$, Jones et al., 1995).

12.4.2 Studies reporting non-significant associations between ozone and ED visits

Four studies found no significant association between ozone and respiratory ED visits (Bates et al., 1990, Castellsagne et al., 1995, Rennick and Jarman, 1992, Kesten et al., 1995).

In the Vancouver study (Bates et al., 1990), Pearson correlation analyses were carried out on the data, and a very good discussion of the results and their meaning was presented. However, more could have been accomplished with this extensive data set, had more rigorous and extensive statistical methods been used. The analysis considered two seasons, summer and winter (6 months each), which reduced seasonal variations in ozone concentrations and ED visits. But this category was too broad to eliminate within-season cyclic variations. SO_4 was measured as a surrogate for particulate matter. CoH was also measured. But the PM metrics evidently were not utilized in the analysis to correct for their potential confounding effects. A correlation between total ED visits and wintertime ozone plus minimum temperature was noted, but is probably spurious, since ozone levels are lowest in winter. The major interpretation for the failure of this study to find consistent associations with ED visits and ozone is considered to be the handling of the confounding by temperature. The authors noted a significant correlation between ozone and temperature (r=0.64 in summer and 0.57 in winter), and the likelihood of confounding by this factor. The authors did not make an attempt to separate the ozone effect from that of temperature. An additional reason may have been the lack of statistical methods to remove longer-term cyclic variations in ED visits that were not related to air pollution.

In Barcelona Spain (Castellsegue et al., 1995), neither ozone nor black smoke (BS) was associated with ED visits for asthma for adults aged 14 to 65 years. The statistical treatment was appropriate for the removal of short and seasonal long term cyclic variations, and temperature was co-regressed with ozone. BS, SO_2 and NO_2 in single-pollutant models were shown to be related to asthma ED visits. Because no correlation coefficients between ozone and other co-pollutants were given, it is not clear whether these pollutants had confounding effects on ozone and asthma ED visits. No measure was taken to control these factors.

In the study by Rennick and Jarman (1992), the authors controlled the effect of seasonal variation on ozone and asthma visits by limiting the study period to ozone season and episode days. On the other hand, this limited ED visits and ozone days to a very small size. The data on the correlation between ozone and temperature as well as other co-pollutants were not reported, and no effort was mentioned on controlling these environmental factors. These limitations likely substantially reduced the statistical power for detecting a significant ozone effect.

In the Toronto study by Kesten et al. (1995), the authors regressed ozone levels against asthma ED visits, without considering an adjustment for the impact of seasonal cyclic variations, weather, day of the week, and co-pollutants, on ozone and ED visits. These environmental factors may have contributed to confounding the ozone effects.

12.4.3 Summary of ED visits

The data on emergency department visits suggest the same conclusion as the hospitalization studies. The results from ED visit studies demonstrate that ozone is correlated with ED visits when cyclic variables, weather (in particular temperature) and co-pollutants have been properly controlled. The studies that did not detect significant results can be explained on the basis of failure to accomplish one, or more, of these objectives. An increase of about 6% to 8.6% in ED visits for asthma is predicted per 10 ppb increase in ozone (1-h maximum), usually lagged one or two days. For a 10 ppb increase in 5-hour average ozone, the increase in respiratory ED visits is 5.6-14.2%, after adjusting for PM, temperature, and other gaseous pollutants. The predicted percentage increase in ED visits is dependent on ozone as cutoff levels rise, from > 60 ppb (26% in children) to > 110 ppb (43% in all ages). As the number of consecutive days in the pollution episode increases, up to about 2 or 3 days, 68% more visits have been observed at ozone concentrations higher than 110 ppb. In one study that examined concentration-response relationship at ozone levels from 80 to 110 ppb (1-h maximum), asthma ED visits were evidently dependent on ozone concentrations, though only at 110 ppb was the increase significant (White et al., 1994). The positive correlations for ozone and ED respiratory visits, principally for asthma, were observed in four different cities or metropolitan areas in three countries, including Canada.

12.5 FIELD (CAMP AND PANEL) STUDIES

A number of investigators have studied the effects of air pollution, including ozone, by conducting field studies on groups of people engaged in normal activities in the natural environment. Camp studies have the advantage that the subjects, usually children, are free ranging in an environment in which pollutant levels can be closely monitored. In panel studies, a group of subjects (who may be asthmatics) are selected and their medical history and activity patterns and episodes of illness are closely followed. In such studies, pollution exposure can be more accurately gauged than in the general population, and exposures are usually to the ambient mix of pollutants. Endpoints studied were primarily changes in lung function and increased symptoms. This section is based largely on the review by Bates (1994, 1995). New studies published as of April 1997 have been added. A summary of results from field studies is presented in Table 12.4.

12.5.1 Camp Studies

Studies of FEV_1 in children at summer camps in Canada and the USA have indicated that the summer mix of pollutants, including ozone, is associated with measurable declines in function. Kinney et al. (1996) recently evaluated the data sets of six summer camp studies, two in New Jersey (Spektor et al., 1988a,1991), two in Ontario (Raizenne et al., 1989, Burnett et al., 1990), and two in California (Higgins et al., 1990, Avol et al., 1990). Average ozone concentrations (1-hour average at time when lung function measurement) were 53-123 ppb, and the maximum ozone concentrations were 95-245ppb. For each study, regression models were fit relating FEV_1 or Peak Expiratory Flow Rates (PEFR) to ozone.

The majority of the six studies showed significant decrements of FEV_1 in relation to ozone (-0.29 ml to -1.29 ml per ppb ozone, $p<0.05$) (see Table 12.4 for detailed information of each study). There was a wide variation in slopes from the individual studies, and a lack of correlation between the slopes and the means or maxima of ozone encountered in the environment, which may be explained by the different locations, various pollution combinations and gender differences among the camps. The combined six-study data set was used to estimate the mean slopes across all studies for FEV_1 regressed on ozone, with an adjustment for the time-trend in repeated lung function measurements. A pooled slope of -0.26 ml FEV_1 per ppb ozone (SE 0.07, $p=0.0003$) was obtained (temperature not included as a covariate). This was equivalent to a 2.7% drop in FEV_1 for 120 ppb ozone exposure, nearly identical to the 2.8% change observed previously in a controlled chamber study in children exercising for 2.5 hours at 120 ppb (McDonnell et al. 1985a,b). The conclusion was that, on balance, the FEV_1 decrements seen in the camp studies were about the same as demonstrated in the chamber studies.

Additionally, in one of these studies (Higgins et al., 1990), multi-variate regressions were conducted to adjust for temperature, relative humidity and PM_{10}. The multi-variate analyses show that these environmental factors did not substantially affect the slope of FEV_1 per ppb ozone (-0.38 ml/ppb in ozone-only model vs. -0.72 ml/ppb), and ozone remained significantly associated with FEV_1 decrement.

Thurston and his colleagues (1997) studied three groups of children attending a camp for asthmatic children in three consecutive years (1991-1993). The camp was located in the Connecticut River Valley which is frequently downwind of the New York City metropolitan area during the summer months. All medications were kept in a central tent minded by a nurse and a physician. There were 52, 58, and 56 children, respectively, in the groups each year. Average ozone concentration (1-hour maximum) was 83.6 ppb (range 20-160 ppb) for the three years.

Maximum temperature. relative humidity, sulphate and H+ were also measured and were found closely correlated with ozone (r=0.86, -0.52, 0.74, and 0.64, respectively). Health outcomes (medication use, PEFR, head and chest symptoms) were regressed on ozone, sulphate and H+.

Air pollution was found to be significantly and consistently correlated with acute asthma exacerbations, chest symptoms, and lung function decrements (Thurston et al., 1997). For ozone-only model, there was a 0.96 l/min decline (or a 0.3%) in PEFR for a 10 ppb increase in ozone. Chest symptom counts (0.031 symptoms/day/child/10 ppb) and medication use (0.02/day/child/10 ppb) were also significantly associated with daily 1-hour maximum ozone concentrations. When temperature was co-regressed with ozone, the changes in PEFR, medication use and chest symptoms in response to an increase in ozone concentration remained significant.

Exploratory regressions including multiple pollutants were also conducted to further investigate the relative roles of the pollutants (Thurston et al., 1997). In the case of PEFR, the ozone coefficient was virtually unchanged, whereas sulphate declined noticeably. For medication use, the ozone coefficient declined and became nonsignificant. For chest symptoms, the ozone coefficient remained unchanged and significant. In general, these various exploratory multipollutant analyses indicate that ozone is the air pollutant most strongly and consistently associated with adverse health effects in this population of children with asthma.

Spektor et al. (1991) concluded that camp studies generally yield higher effects of ozone than chamber exposures for four possible reasons:

- because the exposures in the field are longer;
- because there may be potentiation by other factors;
- because there may be persistence of effects from the prior day's exposure; and
- there may be persistence of a transient response associated with the daily peak exposure.

The authors cautioned: "It follows that projections of likely effects in the real world from controlled chamber studies should either have a large margin of safety, or the judgment of the extent of effects likely to occur among populations should be based directly on the effects observed in field studies".

Adults jogging in their lunch hour were studied by Spektor et al. (1988b) in Tuxedo, NU. Ozone concentrations (1-hour maximum) ranged 21-124 ppb. Many of these joggers were found to have ventilation levels in excess of 60 L/min (they had selected their own exercise level). Changes in FVC and FEV_1 were related to the ambient ozone on the day of their jogging. The mean slope of FEV_1 decrements across all subjects was -1.35 ml/ppb (SE 0.35). No symptoms were reported by subjects, and no persistence of effects were seen. The authors speculated that acid aerosols might have contributed to the decline of lung function, but no analytical data were reported.

12.5.2 Panel studies

In the early 1970s, Linn et al (1976) carried out an extensive series of studies in Los Angeles using a mobile van which contained an exposure chamber and pulmonary function testing equipment. After an initial finding that suggested that function decrements in the natural environment with photochemical pollutants was greater than that found in chamber exposures, they finally concluded that the observations of decreased function were explicable on the basis of the total ozone exposure. Later studies of competitive cyclists in the same mobile facility (Avol et al., 1984,1985) showed that FEV_1 declines occurred at ozone levels of 160 ppb (a result in accord with the controlled exposure data described above). They concluded that the decrement in lung function in the Los Angeles atmosphere was attributable to the ozone present.

Lebowitz et al. (1985) studied panels of asthmatics and others in Tucson, Arizona drawn from 117 white families from a symptom-stratified sample. Detailed measurements of air pollutants, pollen, bacilli, fungi and algae were made in and around a random cluster sample of 41 households. Thirty-five asthmatics provided daily peak flow measurements. The very complex resulting data showed that both ozone levels and temperature had effects on the peak flow data. The exact ozone data were not reported; instead the data were stratified into <38 ppb, 38-51 ppb, >51 ppb bins. Maximum temperature was also grouped into <61°F, 61-80°F, and 80-96°F. PEFR was expressed as standard deviation scores to remove the effects of age and sex. In each temperature group, average PEFR was found to decrease in an ozone concentration-dependent fashion. The decrement of PEFR was statistically significant. After an adjustment for smoking, indoor TSP, relative humidity and gas stove usage using multi-factorial analysis of variance, outdoor ozone remained significantly associated with PEFR.

Javitz et al (1982) reanalyzed a previous study of 286 subjects with asthma, and chronic bronchitis (probably with and without accompanying emphysema) in Houston, Texas. Daily symptom diaries were kept, and home spirometry testing was done in about one third of the subjects. Respiratory symptoms and medication use increased as the daily ozone maxima increased. In the same city, Holguin et al. (1985) conducted an asthma panel study. They carefully defined an 'asthmatic attack', and followed the panel for six months. Ozone levels ranged up to 270 ppb. They showed that an increase in the 1-hour maximum ozone level of 100 ppb increased the attack probability from a baseline value of 10% to 16%. This 60% increase in risk was four times that observed by Whittemore & Korn (1980) for a panel study of asthmatics in Los Angeles. In Whittermore and Korn's study (1980), they studied adult and child asthmatics living in six different communities in the Los Angeles area. Asthma symptoms were reported by the subjects. The ozone coefficient from the logistic model for daily high-hour ozone was 0.00166 (SE 0.00072). This value is equivalent to a RR of 1.0017 (SE 0.00072) per ppb ozone.

Gong (1987) studied 83 asthmatics in Los Angeles between February and December 1983. Ozone concentrations (1-hour maximum) were 10-110 ppb in 103 days, 350-380 ppb for 3 days. He reported that 39 of the subjects were "ozone responders" (top quartile of respiratory measures), with PEFR and symptoms significantly related to ozone levels. For the whole group, results had not shown a significant relationship. The cases were relatively mild, since 77% of the total group had peak flow measurements within the normal range.

Castillejos et al (1992) reported studies on a panel of normal children in Mexico City, where the daily maximum 1-h ozone level exceeded 120 ppb on 74% of days. This study showed that the FEV_1 and $FEF_{25\text{-}75}$ decrements were strongly related to ozone levels averaged over 24 to 168 hours prior to spirometry. The relation of ozone in the previous hour to the lung function decrements was minimal. For example, FEV_1 slope was -0.592 (SE 0.109) ml/ppb for previous 48 hour ozone. For previous hour ozone, only FVC slope was significant, –0.059 (SE 0.23) ml/ppb ($p<0.05$). Temperature and RH reduced ozone effects. The authors suggested that the results might reflect an inflammatory response in the airways as opposed to an acute physiological response. One-hour average ozone levels in the hour preceding the tests had ranged up to 287 ppb, with a mean of 99 ppb.

Romieu et al. (1997) examined a panel of 67 children known to have asthma and registered at an allergy clinic southwest of the Mexico City. The panel was followed with daily diaries and twice daily peak flow measurements. Pollution levels were known from a monitoring station 200 m from the clinic. The 1-h maximum ozone level was between 40 and 390 ppb during the study, and PM_{10} was between 1.2 and 126 $\mu g/m^3$. The correlation between ozone and PM_{10} was high ($r=0.91$). When temperature was accounted for, a 50 ppb increase in ozone was significantly associated with an 8% increase in cough, a 24% increase in phlegm, an 11% increase in an index of lower respiratory symptoms, and 3% increase in medication use (all $p<0.05$). For PEFR, the decrement was most significant ($p<0.05$) on the second day, with a 2.32 L/min decrease per 50 ppb ozone. When PM_{10} and temperature were accounted for, ozone effects on symptoms (cough 10%, phlegm 29%, lower respiratory symptoms 12%) and PEFR (-2.75 L/min per 50 ppb) were almost the same as without the adjustment, $p<0.05$.

In a study in The Netherlands (Gielen et al., 1997), sixty one children aged 7-13, of whom 77% were taking asthma medication were followed. Peak expiratory flow rate (PEFR) was measured twice daily with miniWright flowmeters at home. Occurrence of acute respiratory symptoms and medication use was registered by the parents daily in a diary. Maximum 1 hour ozone never exceeded 130 $\mu g/m^3$ (65 ppb), 8-hour average ozone was 67.0 ppb (range 27.6-110.8 ppb), 24 hour Black Smoke was not higher than 41 $\mu g/m^3$ and PM_{10} was below 60 $\mu g/m^3$. Correlation between pollutants was moderate ($r<0.3$ between ozone and particles). Temperatures were moderate (8-22° C) during the study period, and did not seem to have significant influence on the outcomes. After adjusting for pollen, time trend, day of week, and particles, PEF index had the strongest association with ozone lagged 2 days, with a decrease of 1.86% (95% CI –3.58% to –0.14%) per 83.2 ppb in the morning and a decrease of 1.88% (-3.94% to 0.18%) per 83.2 ppb in the evening. Eight-hour average ozone was also associated with upper respiratory symptoms, with a RR of 1.23 (95% CI 1.03-1.43). Ozone was not significantly associated with bronchodilator use. The authors concluded that in this panel of children, most of whom had asthma, relatively low levels of particulate matter and ozone in ambient air were able to increase symptoms and medication use, and decrease lung function.

Brauer and Vedal and their colleagues have conducted several studies in the Fraser Valley, which is inland from Vancouver, B.C. They followed a cohort of 58 workers in the fields picking raspberries (Brauer et al., 1996a). These people were at work from dawn till dusk. Their spirometry was measured each morning before starting work, and each evening when they had finished. There were local ambient monitors for ozone and particulate matter. The 1-hr daily maximum ozone had a mean of 40.3 ppb, with a single highest value of 84 ppb. Acid aerosol (3.1 nmol/m3), SO_2 (1-hour average <52 ppb) and NO_2 (1-hour average <28 ppb) were low during the study period, and were therefore not considered in the study. $PM_{2.5}$ mean was 11.4 $\mu g/m^3$. Ozone for the workshift time had a mean of 26 ppb, and a maximum of 54 ppb. Temperature and ozone were highly correlated (r=0.85). The mean FEV_1 fell -3.3 ml and the FVC fell -4.7 ml for each ppb increase in hourly maximum ozone. Deficits were still apparent on following morning. Over the 60 days of work, there was a steady fall in mean FEV_1 of the whole group, with an average 4 ml per day decline. Based on stepwise regression analyses to include sulphate, NO_3 and NH_4 in the models, ozone was still significantly associated with decreased lung function.

The following year, the study was repeated (Brauer et al., 1996b). There were 50 farm workers all of whom were of Punjab origin. Daily spirometry was conducted before and after work; 12-16 hour workdays; the study extended from July 1 - August 18, 1994. The mean of the daily 1-hour maximum of ozone was 39 ppb (range 10-89) and the mean daily maximum 8-hour ozone was 31 ppb (range 5-66). PM_{10} concentrations were low at a mean 24-hour average of 16 $\mu g/m^3$ (but were correlated with ozone r = 0.88). Observed decrements in FVC and FEV_1 were associated with ozone level. The associations were still apparent the following morning, suggesting a persistent air pollution effect. During both summer studies a marked seasonal decline in lung function was observed, but initial values had improved to their original level by the time the second study was done. In 12 subjects studied both years, there was no correlation in individual responses to ozone between the two periods. There was no significant aerosol acidity, but aerosol nitrates were present. Ozone meters were 5 km from farm 1, and 10 km from farm 2. Removing the period of the highest ozone episode did not alter the data. There were 5 possible asthmatics in the group of 50.

These studies are important in the context of standard setting. The Fraser Valley observations represent an exposure pattern that could hardly be replicated in a controlled chamber exposure, since a pattern of ten hours a day of controlled exposure, for 60 consecutive days, together with light exercise, would hardly be feasible. The results indicate that outside work in this atmosphere, in which particle levels were low, and hourly ozone maxima never exceeded 80 ppb during the second year of the study, is associated with an induced function decrement.

12.5.3 Summary of field studies

Field studies examine acute changes of lung function and symptoms of healthy or asthmatic children and adults. Twenty field studies were reviewed in this document, nineteen of which showed a significant association of ozone with lung function decrements and increased symptoms and/or asthma medication uses. Many studies used single pollutant models without adjusting for the potential confounding of co-pollutants. Five studies evaluated multi-pollutant effects, and found ozone effects remained significant when adjusted for PM. Six studies adjusted for temperature and found that the ozone effect persisted.

Table 12.4 Summary of results from field studies

Location and references	Ozone concentration	Health endpoints	Results	Co-pollutants
New Jersey Spektor et al., 1988a	1-h avg. when conducting lung function tests: 53 ppb 1-h max.: 113 ppb.	Camp, 91 healthy children, lung function	Slope for afternoon FEV$_1$: -0.5 ml/ppb, SE 0.16, p=0.002	PM$_{2.5}$, PM$_{15}$, sulphate, H+, temperature were measured too. No multi-variate analysis done.
New Jersy Spektor et al., 1991	1-h avg. when conducting lung function tests: 69 ppb 1-h max.: 137 ppb.	Camp, 46 healthy children, lung function	Slope for afternoon FEV$_1$: -1.29 ml/ppb, SE 0.27, p=0.0001	Temperature and H+ not correlated with lung function changes. No multi-variate analysis done.
Lake Couchiching, Ontario Burnett et al., 1990	1-h avg. when conducting lung function tests: 59 ppb 1-h max.: 95 ppb.	Camp, 29 healthy female children, lung function Asthmatic children, lung function	Slope for afternoon FEV$_1$: -0.19 ml/ppb, SE 0.44, p=0.66. FEV$_1$ decrements were significant on 2 episode days for methacholine-nonresponsive children.	-
CARES, Ontario Raizenne et al., 1989	1-h avg. when conducting lung function tests: 71 ppb 1-h max.: 143 ppb.	Camp, 112 healthy children, lung function	Slope for afternoon FEV$_1$: -0.29 ml/ppb, SE 0.10, p=0.003	Also see effect of H+, but no multi-variate analysis done.
San Bernardino, CA Higgins et al., 1990	1-h avg. when conducting lung function tests: 123 ppb 1-h max.: 245 ppb.	Camp, 43 healthy children, lung function	Slope for afternoon FEV$_1$: -0.84 ml/ppb, SE 0.20, p=0.0001 Slope of FEV$_1$ for previous hour ozone: -0.38 (SE 0.09) ml/ppb, p<0.01.	+Temperature, PM$_{10}$, RH in multi-regression: ozone slope FEV$_1$ decremen= -0.72 ml/ppb (SE 0.15), substantially larger than single pollutant models.
Pine Springs, CA Avol et al., 1990	1-h avg. when conducting lung function tests: 94 ppb 1-h max.: 161 ppb.	Camp, 295 healthy children, lung function	Slope for afternoon FEV$_1$: -0.32 ml/ppb, SE 0.13, p=0.013.	-
New York State Thurston et al., 1997	1-h max.: 83.6 ppb (range 20-160 ppb)	Camps, n=52, 58, & 56 for each year, asthmatic children, symptoms & medication use	PEFR: -0.96 l/min (or a -0.3%)/10 ppb, p<0.05. Medication use: 0.02/day/child/10 ppb, p<0.05. Chest symptom counts: 0.031 symptoms/day/child/10 ppb, p<0.05. + temperature: the changes in PEFR, medication use and chest symptoms in response to an increase in ozone concentration remained significant, values not reported.	+sulphate: PEFR: 0.96 l/min/10 ppb (t=-1.16), p>0.05. Medication use: RR=1.018 (t=0.97)/10 ppb, p>0.05. Chest symptoms: RR=1.053 (t=2.84)/10 ppb, p<0.01.

Table 12.4 Summary of results from field studies

Location and references	Ozone concentration	Health endpoints	Results	Co-pollutants
Tuxedo, NY Spektor et al., 1988b	1-h max.: 21-124 ppb	Jogging adults, n=30, lung function, symptoms	Slope of EEV_1 =-1.35 ml/ppb (SE 0.35). No symptoms reported.	-
Los Angeles, CA Avol et al, 1984	153±25 ppb	Panel of healthy adults (competitive bicyclists), n=50, mobile lab study. Symptoms and lung function	Mild increase in lower respiratory symptoms. FEV1 decrements: -5.3%, $p<0.05$, relative to control.	-
Los Angeles, CA Avol et al, 1985	144±43 ppb	Panel of healthy children (12-15 y), n=59, mobile lab study. lung function	Decrements ($p<0.05$) in FVC: -2.1%; FEV_1: -4.2%; $FEV_{0.75}$: -4.0%; PEFR: -4.4%, relative to control.	-
Tucson, Arizona Lebowitz et al., 1985	Micro-outdoor ozone, mean not given. stratified into <38 ppb, 38-51 ppb, >51 ppb	Panel of asthmatics, n=211, lung function	Maximum temperature grouped:<61°F, 61-80°F, and 80-96°F. Average PEF index decreased in an ozone concentration-dependent fashion, in each temperature group, $p<0.05$	Adjusted for smoking, indoor TSP, RH and gas stove usage: outdoor ozone remained significantly associated with PEF index.
Houston, Texas Javitz et al., 1982	-	Panel of 286 asthmatics and chronic bronchitis. Lung function and symptoms	- Respiratory symptoms and medication use increased as the daily ozone maxima increased.	-
Houston, Texas Holguin et al., 1985	1-h max. Up to 270 ppb	Panel of asthmatics. Asthma attack probability	Asthma attach probablity increased 6.0%/10 ppb RR=1.062 (SE 0.023)/10 ppb	-
Los Angelus, CA Whittermore and Korn, 1980	-	Panel of asthmatics Symptoms	RR=1.017 (SE 0.0012)/10 ppb ozone, symptoms.	-
Los Angelus, CA Gong 1987	1-h max. 10-110 ppb (103 days), 350-380 ppb for 3 d.	Panel of mild asthmatics, n=83, symptoms, lung function, medication use	For whole group: 1-h max ozone not related to changes in lung function, symptoms and medication use For "responders" (top quartile of respiratory measures) : ozone related to PEFR and symptoms.	-
Mexico City Castillejos et al., 1992	daily maximum 1-h ozone level exceeded 120 ppb on 74% of days. In the hour preceding the tests ranged up to 287 ppb, with a mean of 99 ppb.	Panel of healthy children, n=148, lung function.	FVC slope =–0.059 (SE 0.23) ml/ppb, $p<0.05$, to previous hour ozone. For previous 24, 48, 168 h ozone, FEV_1 and $FEF_{25\text{-}75\%}$ decreased significantly. E.g. previous 48 h ozone, FEV_1 slope = 0.592 (SE 0.109) ml/ppb.	Temperature and RH reduced ozone effects. No adjustment for other pollutants.
Mexico City Remieu et al., 1997	1-h max.: 196 ppb (range 40-390 ppb)	Panel of asthmatic children, n=67, lung function and symptoms, medication use.	+temperature, PEFR mean (95%CI) L/min/50 ppb: lag 0: -1.81 (-3.6 to –0.01) lag 1d: -2.32 (-4.17 to –0.47) lag 2d: -0.21 (-2.44 to 2.02)	+temperature, PM_{10}: PEFR mean (95% CI): -2.75 l/min/50 ppb (-4.95 to –0.5).

Table 12.4 Summary of results from field studies

Location and references	Ozone concentration	Health endpoints	Results	Co-pollutants
			+temperature, symptoms odds ratio/50 ppb (95% CI), lag 0d: cough: 1.08 (1.02-1.15) phlegm: 1.24 (1.13-1.35) lower respiratory: 1.11 (1.05-1.19) in a concentration-dependent fashion (<120 ppb to >250 ppb). bronchodilator use: 1.03 (1.00-1.05)	Symptoms odd ratio/50 ppb (95% CI): Cough: 1.10 (1.00-1.20) Phlegm: 1.289 (1.17-1.43) Lower respiratory: 1.12 (1.01-1.23)
The Netherland Gieler et al., 1997	1-h max.: 77.3 ppb (33-130 ppb). 8-h avg.: 67.0 ppb (range 27.6-110.8 ppb)	Asthmatic children (61), lung function, symptoms and medication use.	-	1-h max. data not given. +PM_{10}, BS, 8-h avg. ozone: PEF index had strongest association with ozone, lag 2 d: Morning: -0.22% (95% CI –0.43% to –0.017%)/10 ppb. Evening: -0.226% (-0.474% to 0.022%)/10 ppb. RR (95% CI) for upper respriatory symptoms, lag 0: 1.23 (1.03-1.43) RR (95% CI) for bronchodilator use, lag 2 d: 1.16 (0.87-1.45)
Fraser Valley, BC Brauer and Vedal, 1996a	1-h max.: 40.3 ppb (13-84 ppb). Mean of workshift: 26 ppb (8-54 ppb).	Farmers, n=58, lung function	+temperature, day of study, 1-h max. ozone: FEV_1 -3.3 ml/ppb FVC: -4.7 ml/ppb	+sulphate, NO_3, NH_4: 1-h max. ozone was significantly associated with lung function decrements. Values not reported.
Fraser Valley, BC Brauer and Vedal, 1996b	1-h max.: 39 ppb (range 10-89 ppb). 8-h max.: 31 ppb (range 5-66)	Farmers, n=50, lung function	Observed decrements in FVC and FEV_1 were associated with ozone level. The associations were still apparent the following morning, suggesting a persistent air pollution effect.	PM_{10} concentrations were low (24-hour avg. 16 µg/m^3), and were correlated with ozone, r = 0.88.

12.6 CHRONIC EFFECTS

The acute effects of daily fluctuations in ozone on symptoms, lung function, and inflammation are generally considered to be relatively transient and reversible. Evidence that repeated exposures to very low concentrations over long time periods could result in chronic conditions would be viewed in a more serious light, from the perspective of standard-setting, than lung function decrements due to acute episodes of exposure to somewhat higher concentrations. The recent review by Bates (1994, 1995) of cross-sectional and longitudinal studies examining the evidence for the effects of chronic exposure to ozone serves as the basis for this section, with some additions of recently published studies. A summary of the results is presented in Table 12.5.

12.6.1 Cross-sectional comparisons

Cross-sectional studies examine and compare rates or prevalence of diseases or mortality across geographic locations. This type of study has often been applied to the examination of long-term or chronic effects and their relationship to air pollutants.

Hodgkin et al. (1984) found some evidence of more respiratory symptoms in non-smokers in higher oxidant regions, but the difference was not great. Linn et al. (1980) could not demonstrate consistent differences in either respiratory symptomatology or function between populations of office workers in areas with different levels of oxidant pollution.

An interesting comparison has been published of children in Austria living in relatively high and low ozone regions (Zwick et al., 1991). Two hundred and eighteen children (mean age 11.6 years) lived in the high ozone region in which ozone exceeded 100 ppb 9.68% of the time, and 281 children lived in a low ozone region where that value was never exceeded. The time metric of ozone was not given in the text. Other pollutants were similar between the regions, but no measurements of particle concentrations were taken. There were no specific exposure data for any of the children. There were no differences in allergic background, as judged by immunoglobulin (IgE) levels or asthma symptoms; no differences were detected in cough or breathlessness, nor in pulmonary function status, but there was a higher incidence of bronchial hyperresponsiveness to methacholine in the high ozone group (29% vs 21%; $p<0.02$), and differences in the ratios of types of lymphocytes. The 'high ozone' children showed a decrease in T-helper lymphocytes and an increase in T-suppressor cells compared to the children in the low ozone area. T_4/T_8 ratios were decrease by 17.7% ($p<0.001$) and natural killer cells by 12.6% ($p<0.001$), effects which have been linked to immunosuppressive function. Although the significance to the subjects of these hematological differences is unclear, the authors interpreted their overall findings to indicate that ozone had caused a significant difference in status.

Other epidemiological evidence of long-term adverse effects of ozone exposure has come from the analysis of the National Health and Nutrition Examination Survey (NHANES II) data in 44 cities in the US provided by Schwartz (1989). Youths (n=3,922) aged 6 to 24 years, were examined for lung function parameters. Average hourly values for the 365 days preceding spirometry were used. Median average annual hourly ozone concentration was 33 ppb. However, only 25.6% of the subjects lived close enough to a monitor to have ozone exposure assigned to them. The author reported a decrement in FVC in children in relation to calculated long-term ozone exposures as low as 40 ppb annual average. The effect persisted after control for sex, race, age, family income, educational level, chronic respiratory symptoms, and smoking history. However only univariate analysis could be undertaken, and possible co-occurring pollutants could not be simultaneously evaluated.

Ostro & Rothschild (1989) used data from the Health Interview Survey in the US between 1976 and 1981, involving 50,000 households. The independent variables included ozone (1-hour maximum) and fine particles, age, sex, race, education, family income, quarter of the year when the individual was surveyed, marital status, existence of a chronic condition, and temperature. Correlation coefficients between ozone and these variables were low ($r<0.1$), with the exception of ozone and temperature ($r=0.5$ to 0.68 for 6 years). Health endpoints were respiratory-related restricted activity days (RRAD) and minor restricted activity days (MRAD). Using Poisson regression analysis, when RRAD was regressed on ozone alone, or on ozone and fine particles, ozone did not show a significant association with RRAD. For MRAD, when regressed with ozone alone, in 3 of the 6 years studied, MRAD showed a significant association with ozone. Co-regression with ozone and fine particles did not alter the results. Pooling data from 6 years demonstrated that an increase in 1 $\mu g/m^3$ (0.51 ppb) of ozone was associated with a 0.185% increase in MRAD (elasticity of 0.082). Since ozone displayed a significant seasonal pattern, additional analysis was conducted using only the second and third quarters of each year. The overall regression results did not change. This study confirmed earlier observations by Portney & Malloy (1986) who noted a relationship between ozone levels and reduced activity days by combining aerometric and survey data.

Stern et al. (1989) reported a cross-sectional study, conducted in 1983-1984, using second to sixth grade students who resided in Tillsonburg, Ontario (n=735), and Portage la Prairie, Manitoba (n=895). Tillsonburg had significantly higher concentrations of sulphate, SO_2 and particulate nitrate than Portage la Prairie, but NO_2 and PM_{10} differed little. Average annual maximum concentrations of ozone were similar in the two communities (136 ppb in Ontario, 130 ppb in Manitoba), but the elevated ozone levels above 80 ppb happened more frequently in Ontario (30 days) than in Manitoba (3 days). After adjusting for sex, length of residence, parental smoking and education, and gas cooking, small decrements in FVC (-2%) and FEV_1 (-1.7%) were found in the Ontario children compared to the Manitoba children, but the difference was significant. Because ozone and sulphate in Ontario were closed correlated, it was difficult to separate sulphate effects from ozone effects from this study.

Stern et al. (1994) conducted another cross-sectional study in 5 Ontario towns and 5 in Saskatchewan. Children (n=3,945), 7 to 11 years of age, were examined for respiratory symptoms and lung function. Annual mean 1-hour maximum ozone in Ontario was higher (46.3 ppb, 90th percentile 80 ppb) than in Saskatchewan (34.1 ppb, 90th percentile 47 ppb). PM_{10} and nitrate did not vary between the areas, but annual sulphate levels in Ontario were 3-4 times higher than in Saskatchewan. After adjusting for age, sex, weight, standing height, parental smoking and gas cooking, Ontario children had significantly larger decrements in FVC (-1.7%)

and FEV_1 (-1.3%) compared with Saskatchewan children. The adjusted prevalence of respiratory symptoms did not differ in 10 towns. Coincidence of increased ozone and sulphate precludes definite statements concerning ozone effects.

In the past year, a study by Kunzli et al. (1997) showed that long-term exposure to ozone is associated with declines in lung function, even after addressing potentially confounding pollutants. They investigated the feasibility of retrospective assessment of ozone exposure-relevant covariates and derived lifetime "effective exposure" to ozone. Mid- and end-expiratory flows ($FEF_{25-75\%}$, $FEF_{75\%}$) were regressed against effective exposure and ecological lifetime exposure. A convenient sample of 130 University of California Berkeley freshmen, ages 17-21, participated twice in the same tests (residential history, questionnaire, pulmonary function were recorded), 5-7 days apart. Students had to be lifelong residents of Northern (San Francisco) or Southern (Los Angeles) California. Monthly ambient ozone concentrations were assigned based on the lifetime residential history. An "effective time" spent in ozone concentration environments was derived for each residence and age stratum (0-2 y, 3-5 y, 6-11 y, and 12+ y) with the use of questions about "total time spent outdoors" and time spent in "moderate" and/or "heavy" activity. Effective exposure was calculated over the lifetime (ozone concentration x effective time) of each subject. Ozone metrics used were 8-hr averages (10 AM - 6 PM) and "hours above 60 ppb." $FEF_{25-75\%}$ and $FEF_{75\%}$, which reflect small airway function, decreased with both effective exposure and ecologic assignment of ozone exposure. For a 20 ppb increase (interquartile range) in 8-hr ozone, $FEF_{75\%}$ decreased 14% (95% CI 1.0-28.3%) of the population mean $FEF_{75\%}$. The corresponding effect on $FEF_{25-75\%}$ was 7.2% ($p = 0.08$) of the mean. Use of time-activity data to define exposure had no impact on estimates. Negative confounding factors were region (SF vs LA), gender, and ethnicity. Lifetime 8-hr average ozone concentrations ranged from 16 to 74 ppb with little overlap between regions. There was no evidence for different ozone effects across regions. Multi-variate linear regression was run to adjust for PM_{10}, NO_2, temperature and relative humidity. Effects were independent of lifetime mean PM_{10}, NO_2, temperature, or humidity. There was a trend of decrements in FEV_1, whereas those for FVC were inconsistent and small. The strong relationship of lifetime ambient ozone on mid- and end-expiratory flows of college freshmen and the lack of association with FEV_1 and FVC are consistent with biological models of chronic effects of ozone in the small airways. Since the present study was designed as a pilot study, these findings need to be confirmed in a larger sample that is representative of the target population.

12.6.2 Longitudinal studies

Abbey et al. (1991; 1993) have reported on a continuing study of Seventh Day Adventists over 25 years of age (AHSMOG)(non-smokers; n=7,261) resident in California, and who had resided 11 years or more in areas with different levels of oxidant air pollution. In the Abbey et al. study (1991), ozone exposures were corrected for time spent at work and time away from residence. Adjustments were made for the time spent indoors by individuals. The analysis focused on incident occurrence of obstructive airway disease (COPD). Incident symptoms of COPD were significantly associated with hours above several TSP thresholds, but not with hours above any ozone threshold. In the Abbey et al. study (1993), multiple, linear regression was used to evaluate changes in respiratory symptom severity with the TSP and ozone thresholds. When ozone was considered alone, there was a trend toward an increased risk of asthma for each 1,000-hour average annual increment in the OZ10 criterion[5] (number of hours above 10 pphm ozone), RR 2.07, 95% CI 0.98-4.89). Multivariate analyses adjusted for past and passive smoking and occupational exposures. The multiple logistic regression model for OZ10 and asthma showed that RR for asthma was 1.40 (95% CI 0.99-2.34) for a 500-h average annual increment in OZ10 (1977-1987). Multiple linear regression models for ozone and change in severity score for each respiratory symptom complex showed that there was a statistically significant association of asthma severity score with mean concentration of ozone, and with average annual exceedance frequency for cutoffs of 10 pphm and 12 pphm (1977-1987). Stepwise multiple logistic regression for new cases of asthma was run to test the effects of ozone when TSP was adjusted. Both ozone and TSP were significantly associated with change in severity score for asthma. The correlation between the 1977-1987 average annual mean concentrations of ozone and TSP was 0.74, suggesting that it was not easy to separate TSP from ozone effects. Although this study did not take account of the possible confounding effect of fine particulate pollution, it provided significant evidence of worsening of asthma in those living in a cumulatively higher oxidant environment.

New results from the AHSMOG study indicate that long-term ozone exposure can induce new cases of asthma. In an abstract published in the Journal of Epidemiology (Nushino, et al, 1996), the authors reported that there was a statistically significant ($p<0.05$) association between ozone exposure and the development of asthma in men, but not women, with ozone being more important than any other pollutant. In this study, the gender differences may be the result of males spending more time outside in summer than females (males, 18.4 hrs/wk; females, 10.9 hrs/wk, $p<0.001$). These results are consistent with the results previously published by this group (Greer et al, 1993).

Greer et al. (1993) followed 3,914 nonsmoking California Seventh-Day Adventists, for 11 years. No ozone exposure data were reported. Cumulative ambient ozone exposure through 1987 was found to be significantly associated with definite asthma by reported symptoms or physician diagnosis, only in men (RR 3.12, 95% CI 1.61-5.85, per pphm ozone). The correlation coefficient between ozone and TSP was 0.74. Because no adjustment for TSP and other pollutants were mentioned in the text, the confounding effects of TSP cannot be ruled out.

Detels et al. (1987) reported a longitudinal study of non-smoking subjects in different regions of Los Angeles. Lancaster had lower 3 month mean daily peak hourly ozone (100 ppb) than Glendora (200 ppb). This study showed a faster rate of longitudinal decline of pulmonary function in more polluted regions when subjects were re-tested after an interval of five years. No difference in respiratory symptoms was found during follow-up for either community. There was a considerable loss of sample between the two observations, making interpretation difficult. Bresnitz & Rest (1988), in a review of oxidant epidemiologic data, noted difficulties in the interpretation of this longitudinal study. The question of whether the differences in rate of longitudinal decline of lung function could be attributed to sample loss is a difficult one. Lippmann (1989) in his review of the effects of ozone felt that the preliminary evidence from this study could not be dismissed.

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[5] OZ10 is a measure of cumulative exposure, in hours above a value of 10 pphm (parts per hundred million).

Tashkin et al. (1994) examined the relative impact of residential exposure to community air pollution. Current, former and never smokers, residing in three demographically similar communities that differed in air pollution levels, were followed for 5 – 6 years and evaluated for their annual lung function changes. The communities selected were: (1) Lancaster, with moderate levels of oxidants (70 ppb), and very low levels of other pollutants (sulphate 4.3 $\mu g/m^3$, TSP 85 $\mu g/m^3$, SO_2 10 ppb, NO_2 30 ppb); (2) Glendora, with very high levels of oxidants (120ppb), sulphate (11.0 $\mu g/m^3$), NO_2 (100 ppb), and TSP (133 $\mu g/m^3$); and (3) Long Beach, with high levels of sulphate (11.3 $\mu g/m^3$), NO_2 (110 ppb), TSP (101 $\mu g/m^3$), but low levels of oxidants (40 ppb). The authors reported significant decrements in FEV_1 related to residing in areas with high air pollution levels (Glendora and Long Beach). After the adjustment for baseline spirometry, age, height, history of allergy, the odds ratio for having a large decline ($\geq$90 ml/y for never-smoking men, and $\geq$72 ml/y for never-smoking women) in FEV_1, attributable to living in Long Beach and Glendora, was 1.63 (1.63-2.11) for Glendora, and 2.00 (1.53-2.61) for Long Beach, for both men and women. Smoking also had a significant impact on lung function decline. However, from the data of this study, the effects of ozone cannot be separated from those of co-pollutants.

It may be noted that on theoretical grounds, longitudinal studies should be more sensitive indicators of long-term adverse effects of oxidant pollutant exposure, but such studies are very difficult to organize, and it is difficult to avoid loss of a significant fraction of the surveyed population during follow-up. If this occurs, the interpretation of any result becomes open to question.

Kilburn et al. (1992) conducted spirometry on 556 Mexican-American children in Los Angeles in 1984. In 1987, they conducted spirometry on 251 Mexican-American children, including 106 of the children who had been measured in 1984. All pulmonary function test values were standardized for growth by expressing them as percentages of the predicted values based on sex and height. In 1987, the mean values for FEV_1 and FEF_{25-75} were lower by 4.5 % and 13.6 % of the predicted values respectively compared to 1984. Vital capacities were not statistically different than the predicted values (this is an important control for the test procedure). For the 106 children tested on both occasions, FEV_1 was 2.0 % lower than the predicted value and FEF_{25-75} was 7.0 % lower than the predicted value. There were no significant differences between the 1987 mean value for 145 children tested for the first time in 1987, and that of the 106 re-tested children. The authors concluded that the effects might be due to ambient air pollution, but the data in their paper are not easy to interpret, due to lack of reasonable exposure data.

12.6.3 Autopsy data

Some suggestion of effects on respiratory tissues of chronic exposure to high ozone is provided by the autopsy data of Sherwin and Richters (1991), who described changes of severe respiratory bronchiolitis in a high proportion (27%) of autopsy lungs from 107 young adults aged from 14-25 years, who died in the Los Angeles area from non-respiratory causes. Unfortunately nothing is known about the smoking status, other lifestyle factors or occupational history of these subjects. Although this study has not yet been compared to a control region, and the degree of small airway disease has not been measured by quantitative morphometry, it seems likely that the lesion represents an aggravation of the respiratory bronchiolitis known to be a consequence of cigarette smoking. It may be significant that, as noted above, theoretical dosimetric calculations have indicated that ozone deposition in the human lung would be maximal in this region of the lung, and data on ozone-exposed non-human primates indicated that a respiratory bronchiolitis was the principal induced lesion (see chapter 10).

12.6.4 Summary for chronic effect studies

In general, chronic effect studies have not been able to give a satisfactory conclusion as to the long term effects of ozone. Among 6 cross-sectional studies reviewed, all found changes in lung function or symptoms that might be attributed to ozone pollution. Two of the cross-sectional studies examined the effect of other environmental factors and reported that ozone effects were independent of mean PM, NO_2, temperature and humidity. Three studies tried to adjust for the social-economic and life style differences among the communities studied. Since cross-sectional studies investigate the prevalence rather than the incidence of health effects, and several studies showed high correlation between ozone and PM, no definitive conclusion can be drawn from these studies in terms of ozone effects.

Among 5 longitudinal studies reviewed, all of the authors reported findings of a trend or a statistical significance of increased asthma symptoms or lung function decrements that were related to ozone pollution. However, loss of participants during follow-up and lack of control for other pollutants preclude drawing a conclusive relationship between ozone and long term health effects.

Table 12.5 Summary of results from Chronic effect studies

Location and references	Ozone concentration	Outcomes	Results	Co-pollutants
Austria Zwick et al., 1991	95 – 188 ppb, time metric not given	Cross sectional, children living in high ozone and low ozone areas. 281 children in each group. Hyperresponsiveness, symptoms, lung function, lymphocyte function	Between two groups: Symptoms: no differences in cough or breathlessness pulmonary function status: no difference. Hyperresponsiveness: a higher incidence of bronchial hyperresponsiveness to methacholine in the high ozone group (29% vs 21%; $p<0.02$) Lymphocyte function: The 'high ozone' children showed a decrease in T-helper lymphocytes and an increase in T-suppressor cells compared to the children in the low ozone area. T_4/T_8 ratios were decrease by 17.7% ($p<0.001$) and natural killer cells by 12.6% ($p<0.001$).	Other pollutants were similar between the regions, but no measurements of particle concentrations were taken
44 city National Health and Nutrition	Median of avg. annual hourly	Cross sectional. Age 6-24 y from 44	Nonlinear relationship between annual average ozone and lung function with	No control for other co-pollutants.

Table 12.5 Summary of results from Chronic effect studies

Location and references	***Ozone concentration***	***Outcomes***	***Results***	***Co-pollutants***
Examination Survey, USA Schwartz, 1989	ozone: 33 ppb	cities, 1976-1980. Lung function, demographic, smoking, and health co-variate data	threshold at 40 ppb,	The ozone effect persisted after control for sex, race, age, family income, educational level, chronic respiratory symptoms, and smoking history.
Health Interview Survey, USA Ostro and Rothschild, 1989	1-h max.: 41 to 48 ppb, 1976-1981	Cross sectional. 1976-1981, 50,000 households. Subjects aged 18-65 y. lung function.	An increase in 1 $\mu g/m^3$ (0.51 ppb) was associated with a 0.185% increase in minor restricted activity days (MRAD, elasticity of 0.082). Ozone was not associated with respiratory-related restricted activity days (RRAD).	Co-regression with fine particles: MRAD: 0.17%-0.54% increase per 1 $\mu g/m^3$ (0.51 ppb). RRAD: not significant.
San Francisco and Los Angeles, CA Kunzli et la., 1997	Effective ozone exposure, 8-h avg.: 123.1 ppb-hr (median 88, IQR 207).	130 university students, life-long residents in SF and LA. Lung function.	8-hr ozone: FEF$_{75\%}$: -14% (95% CI 1.0-28.3%)/20 ppb FEF$_{25-75\%}$ -7.2% (p = 0.08)/20 ppb	Effects were independent of lifetime mean PM$_{10}$, NO$_2$, temperature, or humidity. +PM, FEF$_{75\%}$: -0.237 L/sec/ppb (SE 0.117) +NO$_2$, FEF$_{75\%}$: -0.257 L/sec/ppb (SE 0.118) +all: FEF$_{75\%}$: -0.173 L/sec/ppb (SE 0.124).
Ontario and Manitoba Stern et al., 1989	Annual mean 1-h max.: 34 to 50 ppb 90th percentile	Cross sectional study, 1983-1984. Second to sixth grade students, n=735 in Ontario, n=895 in Manitoba. Respiratory health and lung function.	Ontario town had more ozone days >80 ppb, 30 days compared to Manitoba town, 3 days; small decrements in FVC (-2%) and FEV$_1$ (-1.7%) were found in the Ontario town compared to the Manitoba town, p<0.05; adjusted for age, sex, height, parental smoking.	High sulphate and ozone correlation, and ozone possible effects were completely confounded with sulphates.
Ontario and Saskatchewan Stern et al., 1994	Annual mean 1-h max.: Ontario: 46.3 ppb (90th, 80 ppb) Saskatchewan: 34.1 ppb (90th 47 ppb)	Cross sectional study, 1985-1986. 7-11 y children, n=3,945, 5 towns in Ontario, and 5 towns in Saskatchewan. Respiratory health and lung function.	Adjusted for age, sex, weight, standing height, parental smoking and gas cooking. Ontario: FVC –1.7% (p<0.05), FEV1 –1.3% (p<0.05) compared with Saskatchewan children. No effect for mid-volume flows, except for subjects with asthma. No effects for symptoms, odds ratios 0.77 (cough) -1.15 (bronchitis), p>0.05.	-Coincidence of increased ozone and sulphate precludes definite statements concerning ozone effects.
AHSMOG, CA Abbey 1991, 1993	Not reported	7,261 Seventh Day Adventists resident in CA over 25 years of age, who had resided 11 years or more in areas with different levels of oxidant air pollution.	a trend toward an increased risk of asthma for a 1,000-hour average annual increment in the OZ10 (number of hours above 10 pphm ozone) criterion: RR=2.07, 95% CI 0.98-4.89.	+smoking, occupational exposures asthma symptoms RR=1.40 (95% CI 0.99-2.34) for a 500-h average annual increment on OZ10 (1977-1987). asthma severity score: associated with mean concentration of ozone (1977-1987), and with

Table 12.5 Summary of results from Chronic effect studies

Location and references	Ozone concentration	Outcomes	Results	Co-pollutants
				average annual exceedance frequency for cutoffs of 10 pphm and 12 pphm (1977-1987). +TSP: jointly was significantly associated with change in severity score for asthma. But ozone itself lost significance. No interaction between TSP and ozone was found.
AHSMOG, CA Greer et al., 1993	Not reported	3914 nonsmoking California Seventh-Day Adventists, followed for 11 years.	Cumulative ambient ozone exposure through 1987: RR (95% CI) for definite asthma by reported symptoms or physician diagnosis, per pphm: men: 3.12 (1.61-5.85),$p<0.05$ Women: 0.94 (0.68-1.34), not significant. Men+women: 1.31 (0.96-1.78).	Between ozone and TSP, r=0.74. Did not control for TSP.
Lancaster and Glendora, CA Detels et al., 1987	3 month mean daily peak hourly values: Lancaster: 100 ppb Glendora: 200 ppb	5-y follow-up study. Non smoking no Hispanic whites, 7-59 years of age.	No difference in respiratory symptoms over follow-up for either community Across all age groups, slope of Phase III of N_2 washout deteriorated more rapidly in Glendora than in Lancaster.	-
Lancaster and Glendora, Long Beach Tashkin et al., 1994	Lancaster: oxidants 70 ppb, sulphate 4.3 μg/m^3, TSP 85 μg/m^3 Glendora: oxidants 120ppb, sulphate 11.0 μg/m^3, TSP 133 μg/m^3 Long Beach: oxidant 40 ppb, sulphate 11.3 μg/m^3, TSP 101 μg/m^3	Never (n=621-763), former (n=317-479) and smokers (n=472-691), 25-59 y, non Hispanic whites, followed 5 y in Lancaster and Glendora, and 6 y in Long Beach, annual lung function changes	Adjustment of baseline spirometry, age, height, history of allergy. A large decline in FEV1 is defined as ≥90 ml/y for never-smoking men, and as ≥72 ml/y for never-smoking women. Odds ratio (95% CI) for having a large decline in FEV1 attributable to living in Long Beach and Glendora was: Men: 1.84 (1.23-2.77) for Glendora, 2.58 (1.69-3.94) for Long Beach Women: 1.48 (1.05-2.09) for Glendora; 1.51 (1.06-2.17) for Long Beach Men + women: 1.63 (1.63-2.11) for Glendora; 2.00 (1.53-2.61) for Long Beach	-
Los Angeles, CA Kilburn et al., 199	Not reported	556 2nd and 5th grade students, Mexican-American. Lung function	Interpretation of results was difficult due to loss of participants during follow-up and lack of reasonable exposure data.	-

12.7 SUMMARY AND CONCLUSIONS

The major emphasis of this epidemiological review has been on the studies of mortality, hospitalizations and Emergency Department visits, because of the more complete information for these endpoints. All of these studies made use of administrative databases in time-series (longitudinal) studies. Environmental or field studies, including camp studies on children and adolescents, and panel or cohort studies on various ages and groups including asthmatics and the elderly, were also considered for qualitative information and coherence with the results obtained for the more serious health endpoints.

12.7.1 Mortality

On balance, the time-series studies examined in this analysis indicate that the association between ozone and mortality is positive, consistent, and independent of other co-occurring air pollutants including particulate matter. Seventeen of the 23 studies examined reported statistically significant positive associations using single pollutant models. Fourteen studies reported results using multi-pollutant models, eleven of which demonstrated statistically significant independent associations between ozone and mortality. These associations were found in cities across North America, in four U.S. and 13 Canadian locations, in Santiago Chile and three European cities, and in a meta-analysis including seven European cities, demonstrating consistency of results despite widely varying climatic conditions, pollutant mixtures, population compositions, and life styles. These associations were reported for cities with mean ozone concentrations (expressed as the one-hour maximum) between 20 and 75 ppb, i.e. below, and in most cases well below the current Canadian Air Quality Objective for ozone of 82 ppb (one-hour maximum).

A meta-analysis was conducted to obtain a pooled estimate of risk. Ten studies that provided suitable quantitative information were selected for meta-analysis based on a list of criteria (see section 12.1.3). Relative risks from these studies were weighted based on their variances, which reflect the size of standard deviations and sample sizes. Seasonal and weather variations and co-pollutants were adjusted in all the selected studies. The weighted mean of mortality risk per 10 ppb increase in ozone (1-hour maximum) was 0.4% (95% CI: 0.19-0.60%).

Using the data from 13 Canadian cities (Burnett, 1998 in Appendix A), the risk for non-accidental mortality is 0.79%/10 ppb increase in daily one-hour maximum ozone (95% CI: 0.59-0.99%). The LOAEL with statistical significance is 20 ppb ($p \leq 0.01$). These values were from single-pollutant models. For mortality, the data show a concentration-dependent relationship, with effects increasing monotonically as concentrations increase. Effects are observed even at very low O_3 levels (down to 10 ppb), although below 15 ppb, the positive associations are not statistically significant. There appears to be no threshold for mortality.

12.7.2 Hospitalizations

The weight of evidence is strong for an association between hospitalizations for respiratory conditions and exposure to ozone at the levels now commonly encountered in Canada. The weighted means of risk of hospitalization for respiratory illness per 10 ppb increase in ozone (1-hour maximum) vary, according to different locations and illness, between 1.8% (95% CI 1.0-

2.6%) for all age respiratory admissions from Canada/New York studies, 1.8% (0.7-3.0%) for all age asthma admissions in Canada/New York studies, 1.9% (1.2-2.6%) for elderly pneumonia, COPD and total respiratory illnesses from US Medicare studies, to 1.14% (0.43-1.84%) from APHEA European studies.[6] These data are from single-pollutant models. (Thurston and Ito, 1999).

For ozone effects from multi-pollutant models, a meta-analysis was conducted for this report by pooling all available data. The criteria for study selection were the same as for mortality studies, except that some populations involved the elderly only. Data include all respiratory admissions, and separate disease categories (asthma, pneumonia and COPD). The weighted mean for respiratory hospitalizations per 10 ppb increase in ozone (1-hour maximum) was 1.12% (95% CI 0.73-1.51%), within the same range as those obtained from single-pollutant models. These studies included all of Southern Ontario, 16 cities in a cross-Canada study, and several U.S. and European cities.

Using the results from 2 Canadian studies (Burnett et al., 1994,1997), a regression analysis was performed for hospitalizations (data from 13 cities, single-pollutant models) (Appendix A, Burnett, 1998). The regression analysis showed that the risk of hospitalization for respiratory diseases is 1.04% per 10 ppb increase in daily one hour maximum ozone (95%CI: 0.78-1.30%). The LOAEL derived from the data is 25 ppb ($p<0.01$). Interestingly, the data show that the regression coefficient between ozone and hospitalization becomes negative between 15 and 20 ppb indicating a possible threshold for hospitalization based on the result of this new analysis.

12.7.3 Emergency Department Visits

The data on hospital Emergency Department (ED) visits generally support the findings from the respiratory hospitalization studies, i.e., increases in ambient ozone concentrations, in the forms of 1-hour maximum, or 5 to 24 hour average, result in significantly increased visits to the Emergency Department due to respiratory illness. To give an example, the percent increase in respiratory ED visits was 6-8.6% per 10 ppb ozone (1-hour maximum), and was 5.6-14.2% per 10 ppb ozone (5-hour average) after adjusting for PM, temperature, and other gaseous pollutants. The association was seen in four cities/metro areas in three different countries (including Montreal), at mean summertime ozone levels (1-5 h metrics) that varied between 30 ppb and 90 ppb. One drawback of the ED visit studies involves the much smaller databases used, when compared with mortality and hospitalization studies. Most of the ED visit studies considered only 1-2 years of data from a few clinics. Many studies tried to control seasonality by limiting the analysis to only high ozone season. Most of the studies considered only asthma-related visits, either of all age groups, children, or the elderly. For studies in which an association could not be shown, the results could usually be attributed to the lack of adjustment for confounding factors, including seasonality, weather, and co-pollutants.

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[6] The findings from Thurston and Ito (1999) were reported as Relative Risk (RR) values per 100 ppb increase in ozone in section 12.4 of this report. Here they are presented as % increase in incidence of the various endpoints, per 10 ppb increase in ozone.

12.7.4 Field (Camp and Panel) Studies

The field studies give convincing evidence that healthy and asthmatic children and adults are affected by ambient ozone pollution at mean levels from 40 ppb (Fraser Valley, BC) to 153 ppb (Los Angeles), reporting increased symptoms and medication use, and decreased FEV_1 or PEFR. Healthy individuals working or exercising outdoors have also been shown to be affected at ozone levels with mean hourly maxima at 40 ppb. Their decline in lung function was consistent with data from controlled exposure studies, but in addition showed a long term decline over the period of 60 days of observation (Brauer et al., 1996a,b). Greater declines in lung function demonstrated from camp studies when compared with controlled exposure studies can be explained on the basis that children in camps are exposed for long periods outdoors, to a pollutant mix, and may be exposed sequentially for several days with insufficient recovery time between daily peaks.

12.7.5 Chronic effects

Recent cross sectional and longitudinal studies demonstrate that there appears to be lung function decrements and the induction of new asthma cases that are associated with long-term exposure to ozone at annual mean 1-hour levels of 34 to 200 ppb. The drawbacks of these studies involve lack of control for co-pollutants and loss of participants during follow-up (in longitudinal studies). In the future, if better designed studies confirm the association between long-term ozone exposure and the development of asthma, this will be an important finding with significant implications for public health.

12.7.6 Effects occurring at low concentrations

The increases in respiratory-related adverse health effects associated with ozone occurred in cities where mean ambient concentrations are well below the current Canadian National Ambient Air Quality Objective for ozone of 82 ppb (one-hour maximum).

The concentration-response relationship analyses in mortality and hospitalization studies show a monotonic increase from ambient levels as low as 20 ppb up to 95 ppb. Increases in Emergency Department visits were also seen at quite low ambient ozone (36 ppb mean for 1-hour ozone in Montreal). The camp studies on children, and panel studies on asthmatics, normal, exercising individuals, and school children, all support this finding.

One interpretation for the substantial sensitivity to ambient ozone concentrations observed in epidemiological studies may be the high heterogeneity of human populations. It is conceivable that there is some small segment of the population at the tail end of the response distribution curve that will react to the stimulus at low concentrations.

12.7.7 Criteria for causality

All of the data considered thus far in this section are ecological in nature, that is, results are based on populations, not individuals, and the exposure of individuals to ozone is not known. It is therefore particularly important to examine these data critically if some idea of causality is to be entertained. The criteria set out by Hill (1965) may give some useful guidance for drawing an inference of causality from association data:

Strength of Association. The associations seen in all the studies are quite weak, in the range of 0.4% (mortality) to 1.9% (hospitalization), to 8.6% (ED visits) for a 10 ppb increase in ozone (1-hour maximum)(a relative risk of less than 1.50, or 50% increase, is considered to be low). They are, however, highly statistically significant in many cases. Inexact exposure information might well have weakened the associations (it is unlikely to have strengthened them).

Consistency. Although the study designs of these time-series studies were similar, the association was seen by a number of investigators in various cities across North America and in several cities in central and South America, all of which differ in their pollutant mix, ozone levels, weather, and socioeconomic status. The 16 city Canadian study (Burnett et al., 1996) included cities from all five regions of Canada. Only two were found to have non-significant associations. The Ontario study by Burnett et al. (1994) was consistent with other studies that had taken place in the same geographic area (Bates & Sizto, 1987; Thurston et al., 1994a,b). Some studies for each endpoint were unable to find a positive association, but their negative results usually could be explained on the basis of the conduct of the analysis, such as lack of controlling for confounding factors, or small sample sizes.

Specificity A number of studies indicated that ozone was the most important of the several pollutants in the mixture, for hospitalizations (Burnett et al., 1994;1996; Schwartz, 1994b, 1995), Emergency Department visits (Weisel et al., 1995; White et al., 1994; Delfino, 1996), and asthma attacks (Javitz et al., 1982; Holguin et al., 1985; Whittemore & Korn, 1980). The hypothesis that H^+ was an important component of the pollutant mixture, possibly necessary for effects of ozone to be seen, was tested in the study by Delfino et al. on Emergency Department visits in Montreal; H^+ was not associated with ED visits for any age group, except for infections in infants (Delfino et al. 1996). Other studies are required to confirm this. Recent data from environments in which aerosol acidity is known to be absent, and in which aerosol sulphates are at very low concentrations, serve to confirm that the primary association is with ozone (Brauer et al., 1996a,b).

Temporality. Most authors investigated the possibility that pollutant levels one or more days before the admission or visit ('lag time') were more important predictors than current day concentrations. Lag times were generally 1 to 2 days for hospitalizations, and perhaps a little shorter for Emergency Department visits, especially if the hospital served as the only source of medical advice, as in areas of low socioeconomic status (White et al., 1994; Romieu et al., 1995). In wealthier areas the family physician might be the first call. Negative lag times were investigated for both control diseases and respiratory diseases by Thurston et al. (1994a,b), and Burnett et al. (1994), and were not found to be associated for the respiratory conditions, but were occasionally associated with other conditions by chance.

Biological gradient. A concentration-response relationship was clearly shown in the Burnett et al. (1994) study in southern Ontario, and one was evident, but not quite so clear in the 16-city national study (Burnett et al., 1997a). Stratification by ozone level was performed in several other studies, but only high ambient exposures resulted in significant elevation of relative risk.

Biological Plausibility. Ozone has been shown in animal experiments and in human controlled exposure studies to result in inflammation, cell necrosis, lowered lung function, and increased airway reactivity. In addition, asthmatics and individuals with 'hyperreactive' bronchi have been shown to be sensitive to the effects of ozone, with pain on deep inspiration, lowered lung function, increased need for medication, and asthma attacks. The progression of these effects to the point where medical attention is sought is quite plausible in light of the above.

Coherence. The data from the three administrative databases on mortality, hospitalizations, and emergency department visits provide a quite coherent picture of progression of effects from high numbers of incidents recorded as ED visits, compared to those who were hospitalized. The slope of the concentration-response curve was steeper for ED visits than for hospitalizations, as would be expected on the basis that an element of choice is involved in the decision to seek medical attention at an Emergency Department or doctor's office, while hospitalizations represent only the most serious cases as determined by a physician. At first glance, there seems to be a lack of coherence when one moves from hospitalizations to mortality, for which the slope was so low as to cast some doubt on whether the effect was real (using the respiratory mortality data). This may be partly explainable on the basis that ozone is associated with respiratory mortality, which is a relatively small part of total mortality (approximately 8% according to a recent economic analysis of Canadian medical care costs). When non-accidental mortality data is selected, or cardiovascular mortality, then the slope is very similar to the one observed for hospitalization data. Farther down what has been referred to as the 'pyramid of effects' (American Thoracic Society 1985), two analyses of relationships of medical care required by asthmatics, one in Winnipeg and one in St. John N.B. (Stieb et al. 1995a,b), showed that asthmatic individuals attended Emergency Departments about five times more frequently than they were admitted to hospital for respiratory disease. Doctors' visits were also shown to be more elevated than emergency Department visits, and days with reduced activity (absences from work or school) were also more frequent. The field or environmental studies also confirm that asthmatic attacks, symptoms, and medication use are increased in a significant portion of the population when photochemical smog is high. An independent analysis has recently confirmed this 'pyramid of effects', and gives some indication of the magnitude of effect that pollution-related increases of only a very few percent, as calculated for ozone, would have on the health care system. In 1990 in

Canada, hospital-days for asthma (about 40% of all respiratory visits), were estimated to be 281,000, and Emergency Department visits were estimated at 182,000 to 697,000 (depending on source of the estimate), while estimates of physician services (based on two physician surveys) ranged from 2 million to 3.6 million, and days in bed and off work or school were estimated at 2.1 million (Krahn et al. 1996).

12.8 Research Needs

- Since most Emergency Department visit studies had limited databases, and investigated only asthma-related visits, future ED visit studies need to expand their databases, and include ED visits for other cardio-respiratory diseases.
- More longitudinal studies should be conducted to examine the long term effects of ozone exposure.
- Most field (camp and panel) studies have used pulmonary function as an indicator for adverse health effects. Clinical studies have shown that pulmonary function changes do not correlate with tissue injury such as pulmonary inflammation. More sensitive biological markers thus need to be developed to detect tissue injury rather than functional changes.
- In field studies personal exposure monitoring should be carried out, in order to determine exactly what levels of ozone susceptible populations are exposed to, and the relationship with health effects.
- It is not clear why ozone causes cardiac mortality - is it via the impact on the respiratory system with subsequent stress on the heart, or is there a direct link with heart disease. Field studies with more sensitive biological markers may be able to shed some light on this question.

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Health Canada Santé Canada

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NATIONAL AMBIENT AIR QUALITY OBJECTIVES FOR GROUND-LEVEL OZONE

SCIENCE ASSESSMENT DOCUMENT

A Report by
the Federal-Provincial Working Group
on Air Quality Objectives
and Guidelines

July, 1999

This document has been divided into a series of files for easier downloading from our web site.

Part 7 of 7

Canada

13 IDENTIFICATION OF REFERENCE LEVELS

Within the NAAQO process, *Reference Levels* are defined as a level or levels, above which there are demonstrated effects on human health and/or the environment. Conceptually, Reference Levels are LOAELS or NOAELs, where these can be defined. For non-threshold pollutants, for which LOAELs and NOAELs as traditionally conceived cannot be defined, statistical LOAELs can be used to help set the RLs. A statistical LOAEL represents the level (concentration) at which statistical significance in the concentration-response relationship is lost. Reference Levels may be identified for several receptors over specific time periods depending on the sensitivity of the target organism or material(s).

13.1 MATERIALS

There is insufficient information on the effects of ozone on materials on which to base a Reference Level. Therefore it is recommended that no Reference Level for materials be developed.

13.2 VEGETATION

13.2.1 Form

Chronic Effects

As discussed in chapter 8, a number of different 'exposure indices' are used that attempt to capture aspects of ambient ozone concentrations relevant to ozone exposure – plant response relationships. It was recommended that the appropriate form of such an index would be one that is cumulative (i.e. hourly concentrations are summed over some period of time) and that emphasizes peak concentrations. The SUM60 index is such an index and was identified as being the preferred index for use in a Canadian regulatory context, for both short-term and chronic exposures. The SUM60 index is calculated by summing hourly ozone over a given period of time (3 days, 3 months) when concentrations are equal to and greater than 60 ppb. In its seasonal form (3 month), the SUM60 exposure index has performed well using U.S. NCLAN data in relating yield loss with exposure. However, there is no biological basis for inferring that hourly average concentrations below 60 ppb are not important in affecting vegetation.

In reviewing the selection of the SUM60 over a similar index, the AOT40, which is used frequently in European studies, the Canadian air quality data for the period 1980-93 were examined to explore the relationship between these two indices. A regression of these two indices confirms a high degree of similarity ($r^2 = 0.97$). Therefore, it was concluded that, from a regulatory perspective, the decision to adopt a SUM60 index as opposed to an AOT40 makes little practical difference in terms of assessing the areas of ozone impact on Canadian vegetation. It can be argued that the difference in the threshold values between the two indices

(40 ppb versus 60 ppb), as well as differences in the area of the peak which is integrated into the dose (the AOT40 is a "censored index" that only sums concentrations above 40 ppb), renders this type of air quality data comparison invalid. However, when the two indices were examined for their performance in relating ozone air quality with crop yield in a subset of the NCLAN database, there was also no clear biological performance advantage of one versus the other. Based on these findings, there was no compelling scientific evidence to favour a decision between an AOT40 and SUM60 index. Therefore, for reasons discussed in chapter 8, the SUM60 was selected as the recommended form of an exposure index for chronic effects on vegetation.

As described in Chapter 8 (Section 8.2.3), a 10 percent biomass loss level is the minimum level of yield loss that can be confidently measured and attributed to ozone exposure under experimental conditions. Loss estimates less than this can be within the range attributable to experimental error. Therefore, the 10 percent yield loss level is selected as the relevant endpoint for assessment of chronic impacts from ozone exposure.

Acute Effects

Given the importance of protecting vegetation from both acute and chronic foliar injuries that may negatively impact crop quality and marketability, the development of a short term index was considered. Seasonal, cumulative-indices may not adequately capture the frequency and episodicity of short-term, high concentrations.

Because there was no systematic attempt within the NCLAN program to draw relationships between ozone exposure and foliar injury, and because the work which forms the basis for the European short-term AOT40s was difficult to translate into SUM60 exposures and to relate to Canadian growing conditions, data from ongoing investigations into foliar injury in Ontario and from the database of air quality ozone monitoring at rural and forested sites across Canada were utilized. Data from field studies in Ontario on two crops, radish and white bean, were available for analysis and quantification of foliar injury impacts in response to exposure to ambient ozone.

The analysis of the radish data identified two reasonable short term exposure indices: the number of exceedances of the exisiting one-hour ozone NAAQO (82 ppb) and a cumulative one day SUM60. Analysis of white bean foliar injury data and air quality data from the year 1995 found that a 3-day SUM60 index performed best as an indicator of air quality associated with foliar injury development. Statistically significant relationships were also recorded for a 1-day SUM60 and the number of exceedances of the current 1-hour NAAQO of 82 ppb, although the latter two indices attributed a considerably smaller percentage of injury severity to ozone. The final evaluation consisted of exploring further the performance of the 1- and 3-day short-term SUM60 indices using white bean data from the period 1985-1995. The 3-day SUM60 was identified as the best performing index overall.

As described in detail in Chapter 8 (Section 8.2.4), assessments of foliar injury are facilitated by the use of a foliary injury index. The Ontario studies used an index that scored foliar injury on a scale of 0 – 100. A score between 1-20 was classed as trace injury, between 21-35 as light injury, between 36-50 as moderate injury, and above 50 as severe injury. A trace level of foliar injury is considered the lowest level of injury that can be reliably quantified and is therefore the recommended endpoint for the assessment of acute ozone effects on vegetation.

13.2.2 Level

Crop Yield

The U.S. NCLAN database for crops, excluding crops grown in California and those not grown in Canada, was used to identify LOAELs for effects of ozone on crop yield. The 3 month, 12 hour SUM60 values corresponding to 10 % yield loss levels in this suite of crops were shown in Table 8.9. Given the degree of inter- and intra-species variability in crop response to ozone, it was felt that selection of a single LOAEL, from the most sensitive of all crops evaluated, as a Canadian Reference Level for effects of ozone on vegetation, would be inappropriate. Instead, a LOAEL range has been identified that represents a conservative estimate of the range of ozone concentrations above which effects are expected to occur on Canadian crops. This range is 5,900 - 7,400 ppb-h (3 month SUM60, ozone measured during the hours of 08:00 – 19:59). This range is derived from the responses of wheat and turnip (Table 8.9).

Tree Growth

Identification of LOAELs for effects of ozone on tree growth were based on studies conducted by the U.S. EPA in the 1980s on the impact of ozone on forest trees of the U.S. via an OTC exposure protocol similar to that of the NCLAN studies on crop yield. SUM60 values corresponding to 10 percent loss of biomass for individual tree species were presented in Table 8.11. As with the LOAELs for crop species, it was felt to be inappropriate to select a single LOAEL as the Canadian Reference Level, given the degree of variability within and among species. A LOAEL range is identified from the responses of black cherry and aspen (Table 8.11) of 4,400 – 6,600 ppb-h (3 month SUM60, with ozone measured during the hours of 08:00 – 19:59).

Foliar Injuries

In the analysis of the 1985-1995 white bean data from Ontario, a number of alternative 1- and 3-day SUM60 levels were explored on an exceedance basis, in an attempt to determine the most appropriate concentration to provide short term protection from foliar injury in white bean. This analysis included 1-day SUM60 values ranging from 300 – 700 ppb-h and 3-day SUM60 values ranging from 500 – 1,100 ppb-h.

The following conclusions were drawn from this analysis:

- foliar injury to white bean crops in southwestern Ontario was found to be very significantly related to ozone exposure over a three-day period during the three week (20-day) period prior to injury assessment
- in the case of the best performing short-term index, the 3-day SUM60, the relationship between exceedances of a range of candidate SUM60 levels and foliar injury was strongest for 700 ppb-h, followed by 500 ppb-h,
- the evaluation revealed considerable variability in the relationship of the SUM60 values with foliar injury; however, it is apparent that as the level of the SUM60 is increased from 500-1,100 ppb-h, the number of cases where greater than a trace level of injury (Foliar Injury Index > 20) occurs, with zero exceedances of the candidate SUM60 value, also increases (Figure 8.6).

These conclusions provide support for a SUM60 LOAEL value at the lower end of the tested range (i.e. 500-700 ppb-h). Given the limited data on which this LOAEL determination is based, it was felt to be inappropriate to identify a single LOAEL value. Instead a LOAEL range for trace foliar injury is identified as follows: a 3-day SUM60 during the daylight period (08:00 – 19:59) in the range of 500-700 ppb-h.

Although both the form (the 3-day SUM60 index) and the range of the LOAEL for acute effects have been developed using data on only two crops (radish and white bean), both of these plants are known to be sensitive to foliar injury development and to be significantly impacted as a direct result of the foliar injury.

13.2.3 Conclusions Regarding Effect Levels for Vegetation

In summary, it is recommended that the cumulative SUM60 index be used in the assessment of both acute and chronic effects of ozone on vegetation in Canada. The SUM60 index is the sum of hourly ozone concentrations equal to or greater than 60 ppb over the daylight period 08:00 – 19:59. The 3-day SUM60 is used for the assessment of acute effects, whereas the 3-month SUM60 is used for the assessment of chronic effects. Given experimental uncertainties, questions around how results from experimental work apply to real-world growing conditions, and the amount of both inter- and intra-specific variability in the response of plant species to ozone exposure, it was felt that identification of Canadian Reference Levels for effects on vegetation was inappropriate. Instead, LOAEL ranges have been identified for acute effects on crops and chronic effects on crops and trees. These represent conservative estimates of ozone concentrations above which effects on Canadian vegetation are expected to occur. That the information base is sufficient for such a conclusion is the collective opinion of vegetation effects experts (Heck and Cowling, 1997; Heck et al., 1998).

The LOAEL ranges for chronic effects, derived from Tables 8.9 and 8.11 of this document, are as follows, based on agricultural crops and tree species:

Time Period	SUM60 range (ppb-h)	
	crops	trees
3 month daylight hours (08:00-19:59)	5,900 – 7,400	4,400 – 6,600

The LOAEL range for acute effects, derived from agricultural crops, is:

Time Period	SUM60 range (ppb-h) (crops)
3 day daylight hours (08:00-19:59)	500 - 700

13.3 BIRDS AND MAMMALS

There is insufficient information on the effects of ozone on birds and mammals on which to base Reference Levels. Therefore, it is recommended that no Reference Levels for birds and mammals be developed.

13.4 HUMAN HEALTH

13.4.1 *Form*

Based on the weight of evidence presented in Chapter 12, and reviewed in the following chapter (chapter 14), the epidemiological evidence for mortality and respiratory hospitalization effects at current levels of ambient ozone is significant, consistent, coherent, robust and compelling. Studies on non-accidental mortality and respiratory hospitalization provide quantitative estimates of the health risks of ozone pollution and LOAELs for these endpoints, which are the most appropriate indicators for deriving Reference Levels for ozone.

The number of studies of emergency department visits is limited due to the varying time metrics used (1-hour maximum, 5-, 8- and 24-hour average), and categories of illnesses. Results from these studies were generally consistent with those from the mortality and hospitalization studies. The exposure endpoints were assessed based on 1 to 24 hour averaging times. While qualitatively sound, the quantitative aspects of these studies indicate that it would be impossible to establish a Reference Level using these data.

Measures of other respiratory health effects such as school absenteeism, days of work loss and restricted activity are usually collected through survey instruments, and thus are often subjective. Although these parameters are valid measures of respiratory health, they are not appropriate indicators for establishing a Reference Level for ozone. Small and reversible changes in lung function are measured by spirometry, which in general is a robust measure, but the limited experimental data linking lung function and tissue injury make this endpoint unsuitable for deriving a Reference Level.

The acute effects are, by definition, related to peaks in ozone levels: clinical and population health studies have correlated responses with hourly or longer (up to 24 hour) exposures. A majority of North American epidemiological studies have used 1-hour daily maximum concentrations, and have found a significant association with increased mortality, hospitalization and emergency department visits (see Chapter 12). A few European and Canadian studies have used both 1-hour and 8-hour daily maximum concentrations, and found that the results were highly consistent. One-hour and 8-hour daily maximum concentrations are highly correlated in both the Canadian epidemiological studies and those from other countries. An averaging time of 24 hours is not appropriate because of the strong diurnal pattern exhibited by ozone and the substantial year to year variation in ozone maxima at different sites across the country. Therefore, the averaging time of any target level should be 8 hours or less.

Controlled human exposure (clinical) studies have provided evidence indicating that exposure to ozone at concentrations as low as 120 ppb for 1.5 to 2 hours, or 80 ppb for 6.6 hours, caused pulmonary function decrements and airway inflammation in both asthmatic and healthy subjects. It should be noted that no clinical studies examining injury for 1 to 2 hours of ozone exposure at concentrations below 120 ppb have been documented.

It is noteworthy that a clinical study using varying doses as well as a constant dose over 8 hours (with the same total concentration) has demonstrated that the subjects responded to the varying dose regimen in their pulmonary function decrements almost twice as markedly as the constant dose of ozone. These results suggest that the average dose value calculated as a mean over an 8-hour exposure may underestimate the effect of ozone on pulmonary function induced by a peak exposure.

In view of the results from controlled human exposure and epidemiological studies, it is reccmmended that the ozone Reference Levels be expressed on the basis of a 1-hour daily maximum averaging time.

13.4.2 Level

The ozone Reference Level is defined as an estimate of the lowest ambient concentration at which statistically significant increases in health responses have been detected (i.e. a statistical LOAEL). In general, Reference Levels should not be interpreted as thresholds for affects. In the case of ozone, most studies indicate a continuum of effect through all ambient levels examined, and adverse effects are expected below the Reference Level. However, the analysis performed here (Appendix A) indicates that the statistical strength of the data below the identified Reference Levels is inadequate to provide quantification of effects at lower levels.

The published literature does not provide sufficient information necessary for the derivation of Reference Levels. Instead, regression analyses were performed on mortality and respiratory hospitalization data from 13 Canadian cities over an 11-year period, and LOAELs for these two endpoints were derived (Appendix A). These LOAELs form the basis of the human health Reference Levels for ozone.

The Reference Levels derived from epidemiological studies are supported by animal toxicological findings which have demonstrated that ozone as low as 100 ppb can cause rat pulmonary inflammation. Given that humans have been shown to be 4-5 times more susceptible to ozone than rats, this is equivalent to human exposures of 20-25 ppb. Camp and panel studies which can more precisely characterize local pollution levels, also have provided evidence that ozone at ambient levels can induce asthma symptoms, lung function decrements, and increased asthma medication use. Ideally, one may generate a LOAEL from data of controlled human exposure studies, and ozone has been demonstrated to cause human lung inflammation at concentrations as low as 80 ppb. However, given the fact that ozone-induced lung injury at ozone levels below 80 ppb has not been tested, we are not able to obtain a lowest observable and/or non-observable adverse effect level from clinical studies.

The Canadian data used to derive LOAELs for both total mortality and respiratory hospital admissions are consistent with the data from other published studies. These other studies were conducted in many geographic locations, including cities in North America, Europe and South America, where sources and concentrations of ozone and population composition differ from the Canadian situation. This leads to the conclusion that the data upon which Canadian studies are based are the most representative of the effects of ozone in this country while being within the range of observations from across other geographical conditions, and the most appropriate for the purpose of deriving ozone Reference Levels. Furthermore, the use of raw data from 13 Canadian cities over an 11-year period (Appendix A), and the application of the same statistical treatment throughout, enhance the reliability of the results. Using the same statistical treatment and corrections for confounding factors reduces the uncertainties around any value derived as a Reference Level.

The results of the regression analyses provide assessments for two different types of responses. The LOAEL for the total non-accidental mortality rate is 20 ppb ($p \leq 0.01$), and does not represent a threshold. The respiratory hospitalization rate exhibits a threshold of effect between 15 and 20 ppb of ozone, with a LOAEL at 25 ppb ($p \leq 0.01$).

The lack of evidence of a threshold for mortality precludes the possibility that a sufficiently low level of exposure will be free of any degree of impact. Therefore, the Reference Level, a level above which there are demonstrated effects on human health, is an estimate of the lowest ambient ozone level at which statistically significant increases in health responses have been detected, and not a level below which there are no health impacts.

13.4.3 Recommended Reference Level

Based on the Ozone Science Assessment Document, there is sufficient evidence to conclude an association exists between ambient levels of ozone and human mortality, respiratory hospitalizations and several other health endpoints. The Working Group has developed Reference Levels for the mortality and hospitalization endpoints, as sufficient data exist for the quantification of LOAELs for these endpoints only.

The Working Group notes that this is one of the first instances in which the association between ambient ozone and mortality has been made in the context of a regulatory risk assessment. Although the 1996 US EPA Criteria Document and Staff Paper for ozone did not establish a definitive link between ozone and mortality (US EPA, 1996a,b), the subsequent "Regulatory Impact Analyses (RIA) for the Particulate Matter and Ozone National Ambient Air Quality Standards and Proposed Regional Haze Rule" (US EPA, 1997) noted that the literature on this issue had been evolving rapidly. An extensive review of the new literature on this subject was provided in the RIA report, along with a quantitative analysis of the mortality risk for ozone, concluding that "this new evidence suggests that substantial additional health benefits associated with reducing ozone concentrations may exist" in addition to the benefits associated with other endpoints. The database has continued to evolve since, providing additional evidence of an association between ambient ozone and premature mortality.

Thus, based on the analysis of Canadian mortality and respiratory hospital admission data, the following Reference Levels for ambient ozone are recommended:

Period of Calculation	**Level**	
	non-accidental mortality	**respiratory hospitalization**
Daily, 1 hour maximum	20 ppb	25 ppb

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14 RISK CHARACTERIZATION

Risk Characterization serves an integrative function in a Risk Assessment. That is, the Risk Characterization seeks to integrate the scientific information provided on the nature and concentrations of the "hazard" (in this case, the pollutant ground-level ozone), the nature of the effects induced by exposure to the hazard, and the quantitative relationship(s) between exposure of receptors and the responses they exhibit (i.e. the concentration – response relationships for humans, vegetation and other receptors), into an estimation of the magnitude of impacts expected under current (and future) exposure conditions. This chapter presents the first part of such an analysis. Summaries of the effects described in detail in chapters 7-12 are presented here and the relevant dose – response information is provided where possible. The weight of evidence is evaluated to assess whether the findings support a causal association between ground-level ozone and the noted effects. Uncertainties in the data are discussed, and the research needed to fill the scientific gaps is highlighted. Populations that are most at risk from exposure to ozone are also described. What is not presented in this chapter is the final integration of this information into an estimation of the population risks at current and future ambient ozone concentrations (Risk Estimation). This analysis will be appended to this document as an Addendum.

14.1 MATERIALS

14.1.1 Effects Summary

Although SO_2 remains the most important pollutant in the degradation of materials, other atmospheric pollutants are gaining in importance as a result of declining emissions of SO_2. Ozone is one of these. Ozone damages many different types of materials both functionally and aesthetically, alone, and in combination with other factors. Impacts of ozone alone are most significant for organic materials.

Among the stretched elastomer materials tested, natural rubber, general diene rubber, polyisoprene, polybutadiene, acrylonitrile-butadiene and styrene-butadiene were most affected by ozone. Indeed, one of the earliest techniques used to assess ambient ozone was based on the consistent and rapid cracking of stressed rubber strips when exposed to ambient air. Either the time until cracking or the depth of cracking after a specified time could be related to ambient ozone concentrations (U.S. Dept. of HEW, 1970; Vega and Seymour, 1961). That cracking of rubber can be used effectively as an indicator of ozone concentrations has also been recently confirmed (Serano et al., 1993). Neoprene, silicones, ethylene, butyl rubber and propylene have not been shown to be affected by ozone. The difference in susceptibility of different elastomers is linked to their organic structure, and in particular, to the relative proportion of unsaturated carbon molecules, which are most susceptible to attack by ozone. Protection of elastomers can be increased by the use of antiozonants and waxes. Degradation of elastomers also occurs as a result of exposure to other pollutants and to natural weathering processes; in particular, to sunlight. The importance of these factors relative to the effect of ozone is an ongoing area of research (Tidblad and Kucera, 1996, Lacoste et al., 1994;). Unfortunately, the damaging effects of sunlight can be difficult to distinguish from those induced by exposure to ozone (Yocum and Upham, 1977; Yocum and McCaldin, 1968).

Ozone has the ability to damage textiles by mechanisms similar to those that impair elastomers, with reductions in tensile and break through strength resulting. Synthetic fibers tend to be less affected than natural fibres, such as cotton or silk. Factors such as sunlight, heat, moisture and the presence of micro-organisms can also contribute to reductions in tensile strength, and may be much more important factors than exposure to ozone. However, low levels of ozone can degrade fabrics if they are sufficiently moist. Ozone also causes fading and/or discolouration of dyes. In fact, the primary causal agent of fading is ozone, although significant fading may only occur from exposure to ozone in combination with other factors (e.g. humidity) (NATO, 1974). Lower molecular weight dyes appear to fade most quickly.

Ozone has the ability to embrittle and fade surface coatings by reacting with the organic binder and/or the pigment. Oil based house paints were found to be most susceptible to ozone damage while automotive finishes and paints that contain carbonate filters were the most ozone resistant. Other factors that contribute to paint erosion are temperature, moisture, sunlight, and the presence of other ambient air pollutants. It is likely that the combined effect of these other factors will be larger than the degradation caused by ozone alone.

The impact of ozone on metal and other non-organic building materials is primarily a result of synergistic effects with sulphur dioxide (Tidblad and Kucera, 1996). Metals, such as zinc, silver, aluminum, nickel, copper and iron, are susceptible to corrosion in the presence of both ozone and sulphur dioxide. Ozone concentrations necessary to corrode most metals are greater than typical ambient levels. Corrosion of stone materials, such as marbles, sandstone, limestones, bricks, concrete, and gravel, are also affected by the synergy between ozone and sulphur dioxide. Other environmental factors can also influence the effect of ozone on building materials.

14.1.2 Concentration-Response Relationships

There is no single concentration-response relationship that describes the impact of ozone for all materials. Effect levels and corresponding exposure periods were assessed for elastomers, textiles, and dyes and surface coatings, however no concentration-response relationships were developed. For those materials that experience erosion (surface coatings, metals and building materials), concentration-erosion relationships have been proposed by various authors for specific substances, though they are of varied mathematical form.

Threshold vs. Non-threshold Effect Levels

The mechanism of ozone impacts on materials occurs at the molecular level and therefore precludes there being an effect threshold. The lowest ozone concentrations observed to have a detectable impact are approximately 50 ppb for surface coatings (paints) and textile dyes, and 20 ppb for elastomeric materials and textiles. Impacts on elastomers can occur quite rapidly, while the exposure durations required for impacts to occur on other materials are quite variable. Given the long periods of time over which works of art and intended to be preserved (e.g. 100 years), exposure to low ozone concentrations on a daily basis may be sufficient to induce damage over the long term. No effect level was determined for metals and building materials due to the complex nature of synergistic relationships with sulphur dioxide and nitrogen oxides.

14.1.3 Susceptible Materials

All materials for which literature results were available experienced deleterious impacts due to ozone. Cracking and/or fading or erosion was observed in elastomers, textiles, textile dyes, artist's dyes, surface coatings, metals and building materials.

14.1.4 Mode of Action

Damage to organic materials is caused at the molecular level by chain scissioning and cross-linking mechanisms. In some cases there is an added synergistic degradation of materials due to the presence of other ambient pollutants, specifically sulphur dioxide and nitrogen oxides, and/or high humidity levels.

Elastomeric materials are long chain unsaturated organic molecules. Exposure of an elastomer to ozone results in a breakage of the molecular chain at unsaturated carbon-carbon double bonds. One plausible effect mechanism is that ozone attacks elastomers by adding a chain of three oxygen atoms directly across the double bond, forming a five-membered ring structure. Subsequent reactions lead to a permanently oxidized elastomer (U.S. EPA, 1996).

The mechanism of ozone attack on textiles (and surface coatings also) is similar to that for elastomers. Cellulose fibres (such as cotton or silk) are vulnerable to unsaturated double bond cleavage. Many textile dyes also react with ozone, causing fading. The colour change is the result of ozone molecules breaking the aromatic ring portion of the dye molecule, oxidizing the dye. The daughter molecules that result from this oxidation process could be differently coloured than the parent or colourless. Consequently, the original dye colours become altered or faded (U.S. EPA, 1996). Ozone exposure alone does not usually cause a large degree of fading. Humidity levels of >65% rh are usually required for the fading to be pronounced (NATO, 1974).

Ozone on its own has little ability to affect inorganic materials. However, in combination with sulphur-dioxide, ozone accelerates the corrosive action of sulphur dioxide on metals. The presence of ozone increases the deposition rate of sulphur dioxide to the metal surface and increases the rate of oxidation of the four-valent sulphur to sulphate via a catalytic reaction (Svennson & Johansson, 1993). The formation of the sulphate ion creates the electrolytic solution that has a corrosive effect on protective surface films and on underlying metal that is subsequently exposed. Although this mode of action has been revealed through studies on zinc (Svennson and Johansson, 1993), it is not unlikely that a similar sequence of events will occur with other metals (Lee et al., 1996). Accelerated corrosion of a number of metals has been shown to occur when ozone is present in a sulphur-dioxide containing environment (ICP, 1996; Tidblad and Kucera, 1996).

14.1.5 Uncertainties

Studies conducted in ambient air are prone to the variability of that environment. The variability in the concentrations of co-occurring pollutants obscure the direct ozone impact due to the complexity of potential synergistic relationships. Attempts have been made in some laboratory studies to mimic the ambient environment, via the inclusion of some consequential variables (e.g., humidity, high temperature and UV penetration). Modeling has also been used to approximate damage that would occur in the ambient environment.

For the majority of materials examined, effects were reported qualitatively (e.g., fading/cracking). Even though concentration-response relationships were identified for paints, metals and marbles, the way in which the effects of ozone were quantified was diverse (each relationship predicted either a quantified erosion rate, cracking, or weight-loss). Also, inconsistencies in mathematical expression of the relationship hampered the merging of the results into an overall concentration-response relationship for materials.

14.1.6 Weight of Evidence Discussion

The information available on ozone impacts on materials is consistent in identifying the qualitative impacts. Quantification of the impacts is problematic as a result of variable exposure conditions and durations, the diversity of materials and effects measured, the lack of available concentration-response information for some effects and the issue of potential synergized action of ozone and other pollutants and other environmental variables.

Therefore, it is not possible to define a single concentration-response relationship or effect level for materials. However, it should be recognized that chronic exposures in an ambient environment, in the order of weeks, at concentrations in the range of 20 – 50 ppb, have the potential to adversely impact elastomers and textiles, paints and dyes. Erosion rates predicted for inorganic materials (metals and stone) in response to exposure to ozone in combination with SO_2, are very small. If the results of experimental exposures over several weeks can be extrapolated to longer periods of time, hundreds of years would be required for measurable degradation of metals or stone to occur.

14.1.7 Recommendations

Given the lack of adequate quantitative concentration-response information for ozone effects on materials, it is not possible at this time to attempt any estimation of the risks to materials in the Canadian environment from exposure to ambient ozone.

14.2 VEGETATION

As noted in the Introduction to chapter 8 (Effects on Vegetation), the discussion in this document on the effects of ozone on plants has been based upon the prior report of the Vegetation Objective Working Group (VOWG) of the Multistakeholder NO_x/VOC Science Program (1997). A review of more recent literature indicated that the information base on the effects of ozone on plants had not progressed sufficiently to warrant any change to the discussion or conclusions of the report by the VOWG.

14.2.1 Effects Summary

Ozone injury was first observed and documented under field conditions in the Los Angeles area. The majority of research that followed through the 1950s to the 1970s was conducted with pot-grown plants under greenhouse or controlled environment conditions. It is only since the mid-1980s that research activities have attempted to mimic field conditions more closely through the use of open top chambers and fumigation systems.

Acute symptoms on broad-leaved plants consist of chlorosis, fleck, stipple and uni- or bifacial necrosis. On conifers, acute responses consist of mottle, banding and chlorosis (Krupa & Manning, 1988). Chronic symptoms are related to frequent, relatively low hourly ozone concentrations, with periodic, intermittent peaks of relatively high hourly concentrations. Chronic effects can lead to changes in plant growth, productivity and quality, and these effects may occur without visible symptoms. When symptoms do develop, they can include chlorosis, delayed early season growth, premature senescence and leaf abscission (Manning & Krupa, 1992). In the case of acute effects, plants can compensate for stress during respite periods; therefore, the frequency of ozone episodes and the time interval between such episodes are critical in evaluating and modeling plant response (Krupa & Kickert, 1989; Lefohn & Runeckles, 1987).

It is well recognized that foliage is the primary site of plant response to ozone exposure. It is also known that ozone exerts a phytotoxic effect only if a sufficient amount reaches sensitive sites within the leaf. Thus, ozone injury will not occur if the rate of uptake is low enough that the plant can detoxify the ozone or is able to repair or compensate for the effects (Tingey & Taylor, 1982). Effects at the cellular level are ultimately expressed as visible injury to the leaf or as secondary effects that can be expressed as reduced root growth, reduced yield of fruits or seeds, or both. The main factor in the ultimate impact of ozone exposure on growth or yield of individual plants is whether ozone directly or indirectly impacts a metabolic or physiological process that is or may become a limiting factor in plant growth at the time of exposure.

In recognition that impacts on vegetation may occur in addition to, or in the absence of, visible foliar injury, damage assessment has gained favour as an indicator of plant response to ozone exposure. The concept of damage includes reductions in aesthetic values, the occurrence of foliar injury, and loss of weight, number, or size of the plant part intended for harvest. Loss in yield may also include changes in physical appearance, chemical composition, or the ability to retain quality features during storage. Loss of aesthetic value includes negative impacts on the appearance and marketability of ornamental plants or crops in which the foliage is paramount.

14.2.2 Quantification of Impacts

Effect End Point Selection

There are several end points that may be considered in establishing concentration-response relationships for vegetation. The two most common ones are biomass (or biomass losses) and visible foliar injury. (Note that "biomass" with respect to agricultural crops is measured as the yield of the relevant crop part). Biomass losses are related to chronic exposures and visible injury to acute exposures. Both biomass loss and foliar injury have been investigated in crop, ornamental and tree species. As described in Chapter 8 (Section 8.2.3), a 10 percent biomass loss level is the minimum level of yield loss that can be confidently measured and attributed to ozone exposure under experimental conditions. Loss estimates less than this can be within the range attributable to experimental error. Therefore, the 10 percent yield loss level is selected as the relevant endpoint for assessment of chronic impacts from ozone exposure. Similarly, a trace level of foliar injury (score of 1-20 on the foliar injury scale) is considered the lowest level of injury that can be reliably quantified and is therefore the recommended endpoint for assessment of acute ozone effects on vegetation.

Exposure Indices

For adequately quantifying acute and chronic effects, it is necessary to identify both short- and long-term exposure indices. A number of different exposure indices were reviewed in Chapter 8 (Effects on Vegetation) in terms of their efficacy in describing ozone exposure – plant response relationships and their suitability as management tools. This was done for both acute and chronic exposure indices. The evaluation concluded that the form of an index to protect vegetation should be cumulative (summation of hourly values) and should emphasize peak concentrations. The SUM60, the AOT40 and the W126 are three such indices. The U.S. analysis of the NCLAN (National Crop Loss Assessment Network) data for crop yield loss has focused on the SUM60 as the metric to relate exposure to yield response, whereas much of the European work has used AOT40. Other than these two large databases, there is a vast array of studies, of both acute and chronic exposures, for which neither AOT40 nor SUM60 were or can be calculated due to limitations of available air quality data throughout the study period. Therefore, from the perspective of being able to evaluate the largest, normalized databases available, both the SUM60 and the AOT40 were selected as potential exposure indices to use in quantifying ozone exposure-plant response relationships in Canada. The W126 index was dismissed from consideration on the basis that it was too complex an index to administer.

As described in detail in Chapter 8, the review of these two indices showed there was no compelling scientific reason to favour one or the other of the AOT40 or the SUM60. Therefore, other factors were considered, including the administrative advantages of using an index similar to that used in the United States, and arguments that air quality and plant population characteristics, both factors in studies of the impact of ozone on vegetation, would be more similar between the U.S. and Canada than between Europe and Canada. Accordingly, the SUM60 was favoured over the AOT40 for both short- and long-term impact assessments.

As a final step in the decision to adopt a SUM60 versus an AOT40 index, the Canadian air quality data for the period 1980-93 were assessed to explore the relationship between these two indices. The analysis showed that the SUM60 and AOT40 were highly correlated. Therefore, the decision to adopt the SUM60 index as opposed to the AOT40 index makes little practical difference in terms of assessing the geographical areas where vegetation would be most impacted by ozone in Canada. Consequently, a decision was reached by the Vegetation Objective WG of the Multistakeholder NO_x/VOC Science Program to recommend adoption of a 3month, 12 hr. seasonal SUM60 form for assessing chronic effects of ozone on plants. The VOWG also recommended a 3 day, 12 hr. SUM60 form for characterizing acute effects on plants based on studies in Ontario of white bean and radish. These recommendations have been adopted by the WGAQOG. The WGAOQG notes that based on the evidence presented, the SUM60 appears to perform well as an index of ozone exposure, and that it clearly encapsulates some aspects of plant exposure that are important in the response (i.e. cumulative exposure over a time period and the relative importance of peak concentrations). However, the WGAQOG also notes that there are other factors demonstrably important in determining plant response (e.g. phenology, time of day etc.) that are not accounted for in the SUM60 index. Furthermore, there is no biological basis for assuming that concentrations below 60 ppb ozone are not significant in the plant response (see discussion below and section 14.2.5). In the future it may be possible to develop a more biologically relevant index.

LOAEL Determination – Chronic Effects

The report of the VOWG (Multistakeholder NO_x/VOC Science Program, VOWG, 1997) was directed at answering the question of the most appropriate form and level for a Canadian Reference Level (RL) and National Ambient Air Quality Objective (NAAQO) for vegetation. Consequently, there was limited discussion of concentration-response relationships for different endpoints and different plant species. As a result, both the VOWG report and this Science Assessment Document have focused, as required, on identifying LOAELs, that is, the lowest ozone concentrations that have been shown to induce a response in plants under experimental conditions. As noted above, a 10% yield loss level (chronic effects) and a trace level of foliar injury (acute effects) were identified as the endpoints of interest with respect to LOAEL determination.

Given the paucity of Canadian data on ozone exposure – crop yield relationships, particularly the lack of data amenable to LOAEL determination using the SUM60 index, the U.S. NCLAN database was relied upon. In order to use the data to develop LOAELs in a Canadian context, a subset of the data was analyzed by removing data for crops not grown in Canada as well as those grown in California, where growing conditions differ markedly from those in Canada. The 3 month, 12 hr. SUM60 values corresponding to 10% yield loss levels from this suite of crops were shown in Table 8.9. From these data, turnip and wheat were identified as most sensitive, and a LOAEL range of 5,900 to 7,400 ppb-h was identified. This range excludes a SUM60 level of 2900 ppb-h identified for one particularly sensitive wheat cultivar.

Similarly, based upon the results of studies conducted by the U.S. EPA in the late 1980s on the impact of ozone on forest trees, a 3 month, 12 hr SUM60 LOAEL range of 4,400 to 6,600 ppb-h was identified for 10% biomass loss. This LOAEL range was based upon the response of black cherry and aspen (Table 8.11).

Potential Exposure Estimates

To assess how the 3 month SUM60 LOAEL range for crop yield loss and tree biomass loss relate to ozone levels observed at non-urban sites across Canada, and in bordering U.S. states where some of the NCLAN study sites were located, data from 1980-93 are used to show the distribution of maximum 3 month SUM60s (Figure 14.1). The LOAEL range for crops is presented in the Figure as a reference mark. It is apparent from this graph that:

- Ontario and, to a lesser extent, Québec and New Brunswick are the provinces most severely impacted by levels of ozone in a range where significant crop and/or tree-growth reductions are possible;
- most Canadian SUM60 levels are markedly lower than those in the neighbouring U.S. states;
- potentially damaging levels of ozone have been experienced periodically in several other areas of Canada: Nova Scotia, Manitoba, Saskatchewan, Alberta and British Columbia; and
- Ontario, the most severely impacted area in Canada, has maximum SUM60 comparable with those of the U.S. states; however, the minimum U.S. values are still significantly higher than those of the most severely impacted Canadian province.

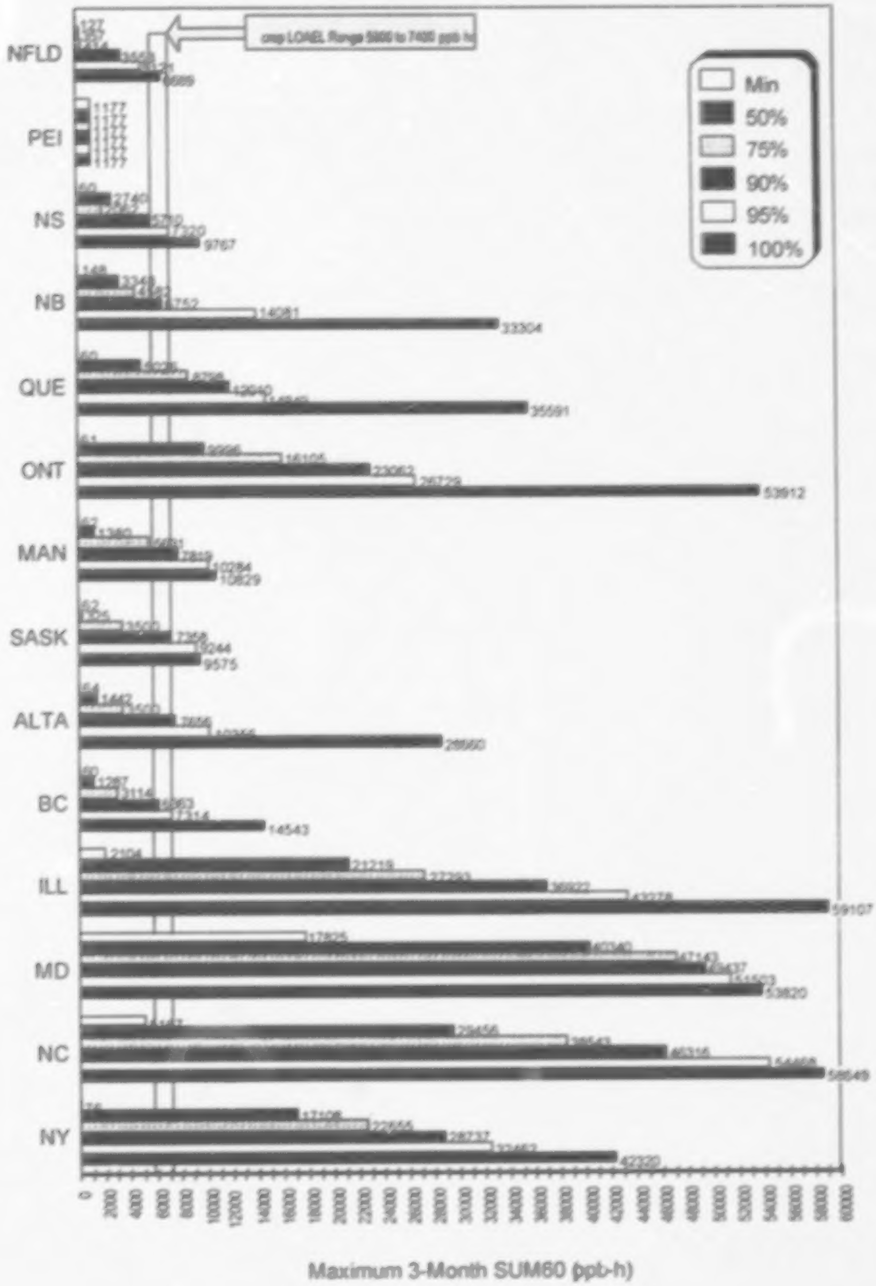
In order to provide a more detailed spatial analysis of the three-month SUM60 values, the data for all rural and forested sites in Canada (plus a few sites in small towns to provide enhanced monitoring coverage) were analyzed in Figures 14.2 to 14.5. The data are contoured to depict the areas impacted on the basis of the mean data for 1988-93, and for a high ozone year (1988).

In each case, the contour limits were based on the following break-points:

- 2,900 ppb-h (100% protection of experimentally evaluated NCLAN crops)
- 6,600 ppb-h (95% protection of experimentally evaluated NCLAN crops)
- 7,400 ppb-h (90% protection of experimentally evaluated NCLAN)
- 12,300 ppb-h (75% protection of experimentally evaluated NCLAN crops)
- 22,400 ppb-h (50% protection of experimentally evaluated NCLAN crops)
- 25,000 ppb-h (proposed alternative U.S. Secondary Standard)

Due to a lack of non-urban monitoring sites, it was not possible to construct contours of SUM60 values for the prairie provinces.

Figure 14.1 Frequency Profiles of Maximum 3-Month SUM60 Values Across Canada and the U.S. (1980-1993)



Contours of 3-Month SUM60 Ozone Levels for Eastern Canada - 1988

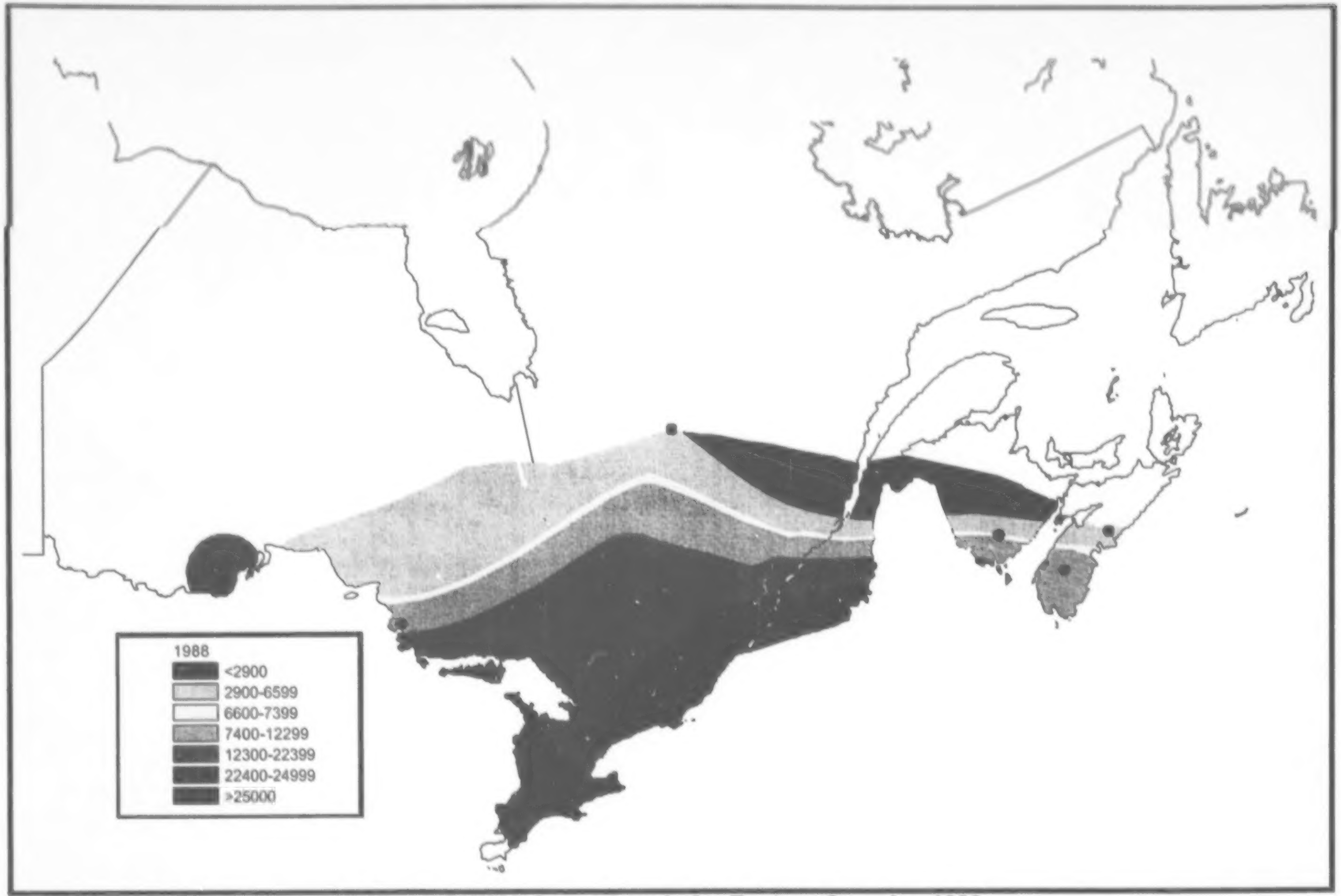

1988
<2900
2900-6599
6600-7399
7400-12299
12300-22399
22400-24999
>25000

Figure 14.2 Contours of 3-Month SUM60 Ozone Levels for Eastern Canada - 1988

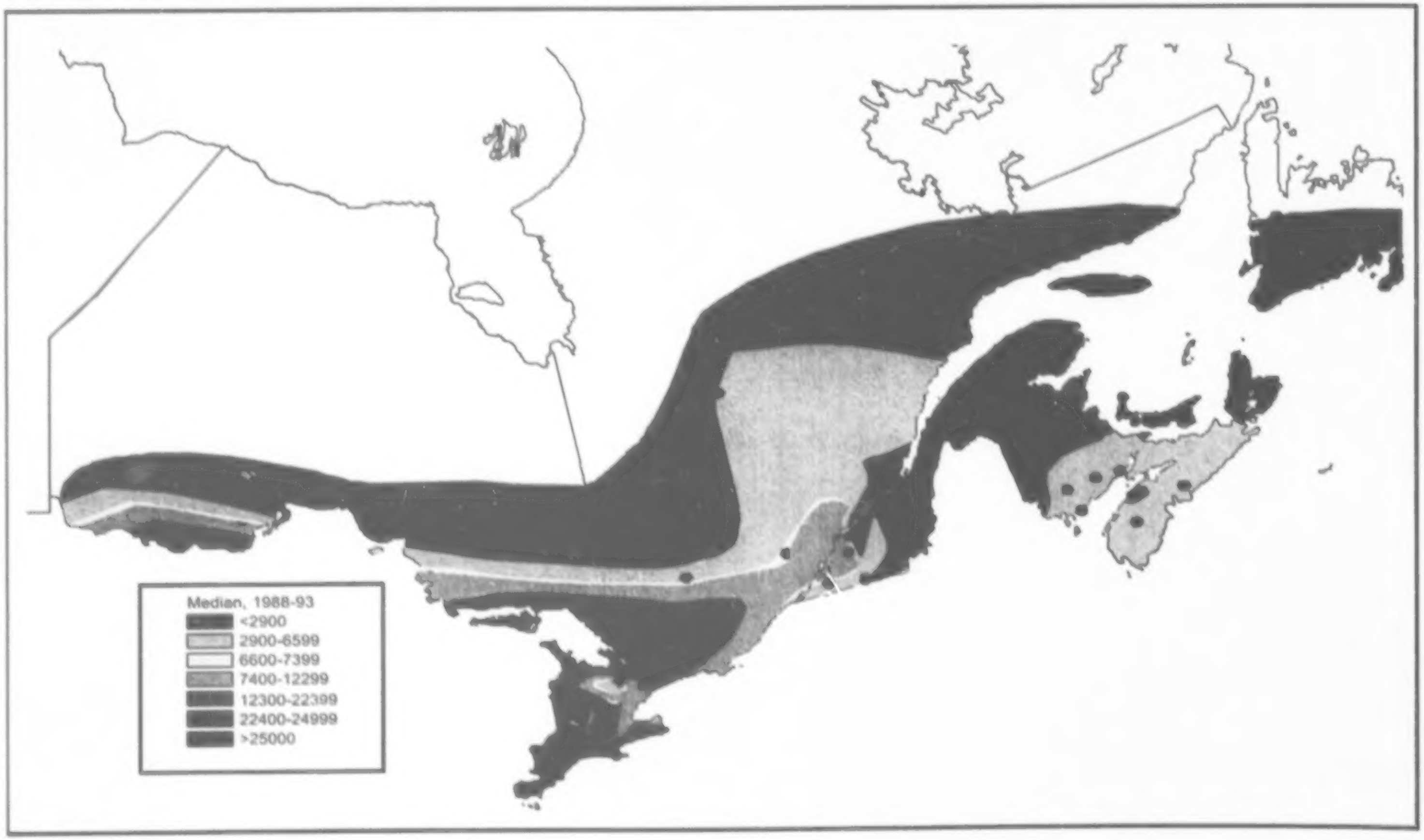


Figure 14.3 Contours of 3-month SUM60 ozone levels for Eastern Canada (Median 1988-1993)

Median, 1988-93
<2900
2900-6599
6600-7399
7400-12299
12300-22399
22400-24999
>25000

Figure 14.4 Contours of 3-month SUM60 ozone levels for British Columbia 1988

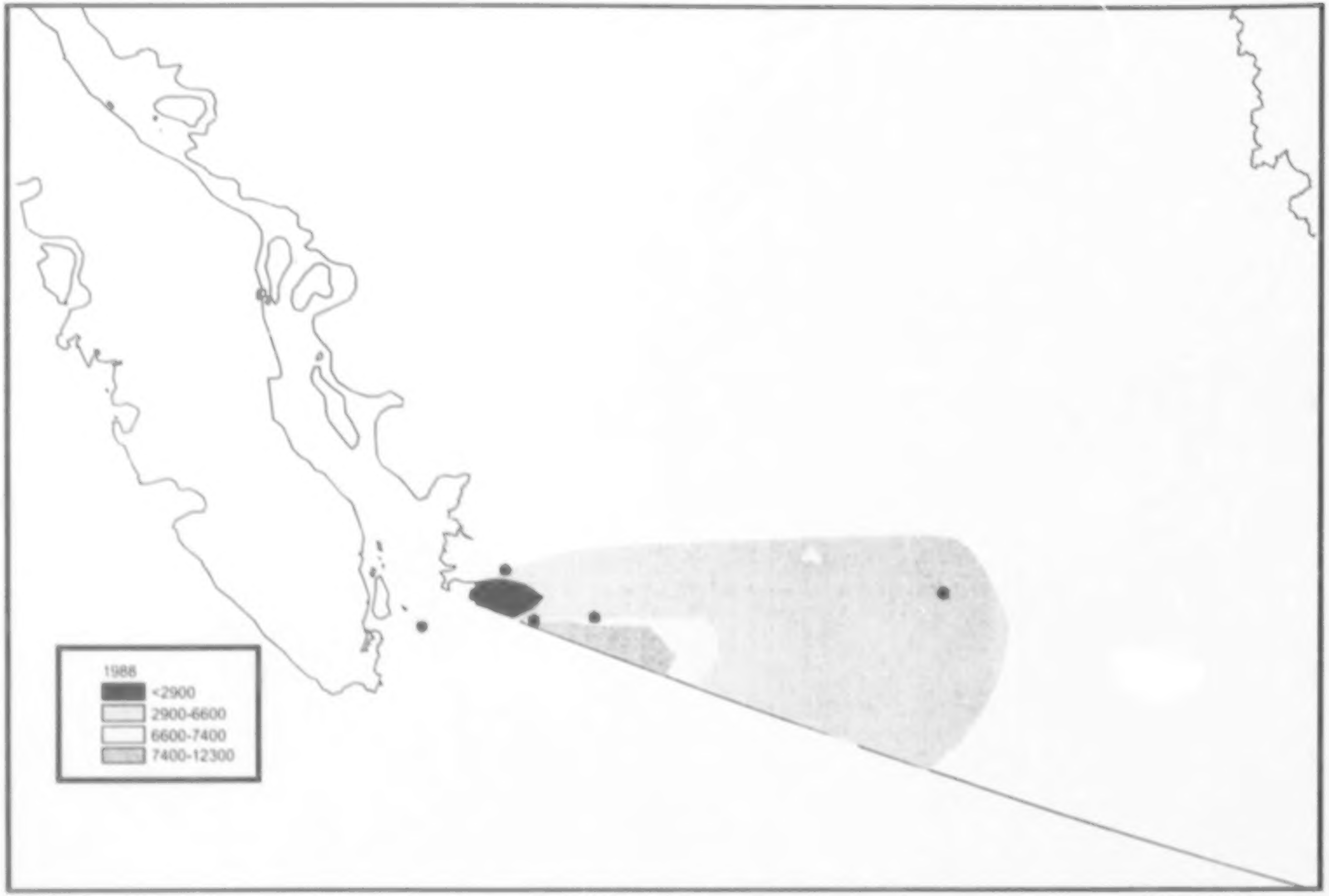
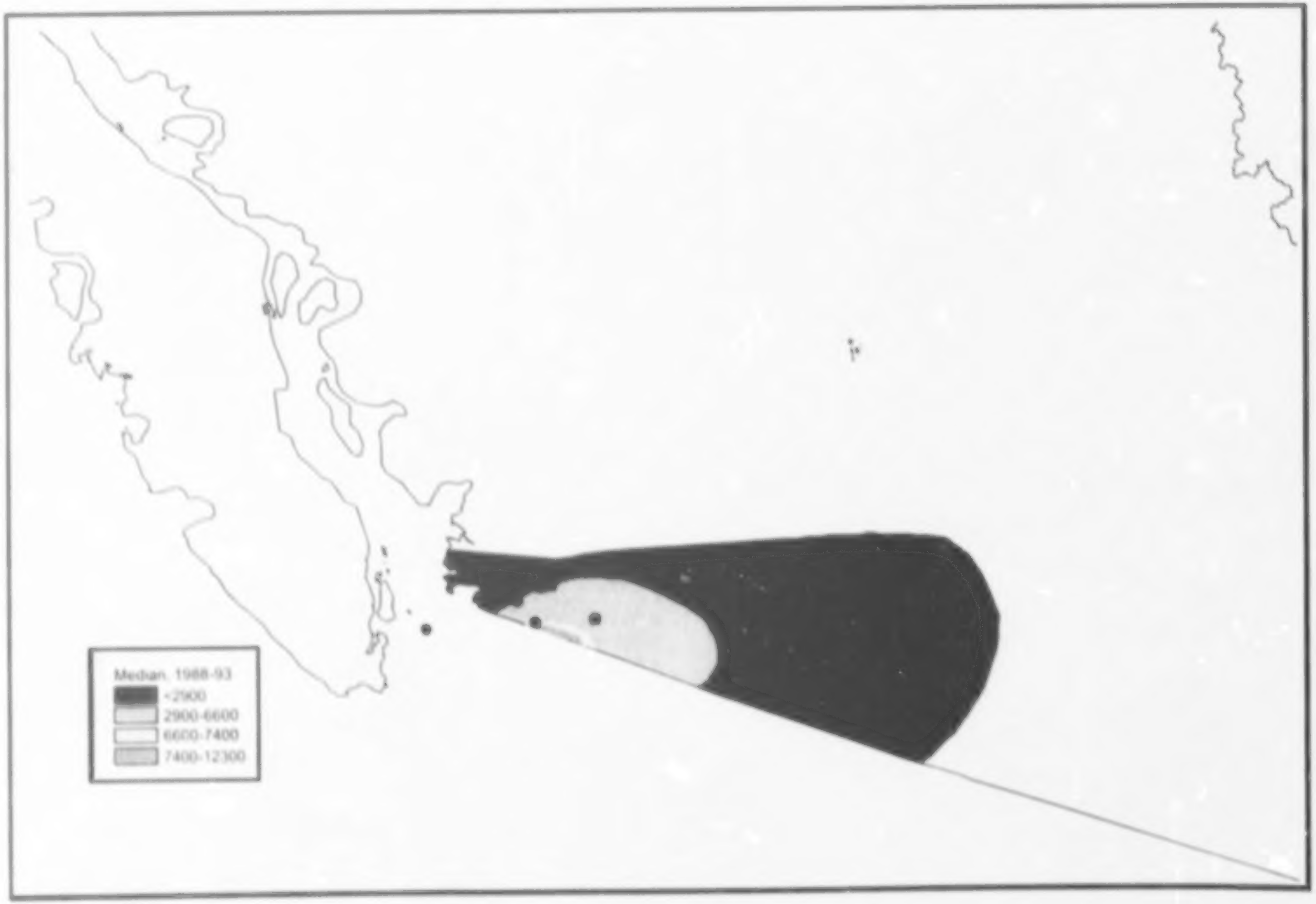

1988
■ <2900
▨ 2900-6600
☐ 6600-7400
▨ 7400-12300

Figure 14.5 Contours of 3-month SUM60 ozone levels for British Columbia (median 1988 – 1993)


Median 1988-93
<2900
2900-6600
6600-7400
7400-12300

LOAEL Determination – Acute Effects

As described in detail in Chapter 8 (Section 8.2.4), assessments of foliar injury are facilitated by the use of a foliary injury index. The Ontario studies used an index that scored foliar injury on a scale of 0 – 100. A score between 1-20 was classed as trace injury, between 21-35 as light injury, between 36-50 as moderate injury, and above 50 as severe injury. A trace level of foliar injury is considered the lowest level of injury that can be reliably quantified and is therefore the recommended endpoint for the assessment of acute ozone effects on vegetation.

Although the history of studies on the acute phytotoxic effects of ozone on plants is a long one, there are, unfortunately, very few studies available that can be evaluated retrospectively to assess ozone exposure – foliar injury relationships using a SUM60 exposure index. The best data available were from studies carried out in Ontario on white bean over the period 1985-1995. These studies identified a LOAEL range for trace injury in white bean of 500-700 ppb-h. Although the recommended form of the short term exposure index was based on analysis of only two crops (white bean and radish), and the LOAEL range was derived from only the white bean studies, both these plants are known to be sensitive to foliar injury following exposure to ozone. Clearly though, there is currently inadequate information to fully characterize the risk of acute foliar injury to crops, trees and native vegetation across Canada.

14.2.3 Susceptible Species

Exhaustive lists of plant foliar sensitivity/resistance to ozone under short-term, controlled-environment conditions have been published (Guderian et al., 1985; Heck et al., 1977). However, there is uncertainty surrounding the relationship between plant foliar injury and life cycle yield and biomass alterations resulting from season-long ozone exposure under field conditions.

Canadian programs have assessed foliar injuries in response to ozone exposure in a variety of agricultural crops. Sensitive crops were identified in New Brunswick (potato), Québec (dry bean, soybean, tobacco), Ontario (dry bean, soybean, potato, tomato, onion, tobacco, cucumber, grape, peanut, radish) and British Columbia (pea, potato). Although these studies were not designed to determine the exposure threshold for foliar injury in all cases, injuries were observed in locations where hourly ozone levels exceeded the current one-hour Canadian objective of 82 ppb for one or more hours prior to the investigation.

In Ontario, studies of the impact of ozone on crop yield have identified the following crops to be at greatest risk: dry bean, potato, onion, hay, turnip, winter wheat, soybean, spinach, green bean, flue-cured tobacco, tomato and sweet corn (Pearson, 1989). Crops estimated to be marginally at risk (insufficient data did not permit more accurate quantification of loss) included cucumber, squash, pumpkin, melon, grape, burley tobacco and beet. In Alberta, the crop yield analysis consisted of a review of the available literature for ozone response based on crops grown. This information was then compared with a limited amount of urban ozone-monitoring data, and it was concluded that there were no identifiable risks to sensitive crops at that time

(Torn et al., 1987). Other agricultural crops commonly grown in Canada but not mentioned above should not be considered resistant to the impact of ozone—their response is simply not known at this time.

Tree species common to Canada that have demonstrated ozone sensitivity with respect to a variety of endpoints (e.g. biomass, height, photosynthesis) under controlled ozone exposure conditions include: maples (sugar, silver, red), ash (white, green), spruce (white), white pine, poplar (hybrid), cottonwood, cherry, walnut, sycamore, white birch and red oak. Although ozone impacts varied significantly, and included both positive (growth stimulus) and negative (growth reduction) responses in many of the experimental studies, the response to seasonal mean exposures of 40–60 ppb for over half of the studies was reported as at least a marginal growth reduction (Pye, 1988). There is also considerable evidence that ozone can injure many annual and perennial grass species commonly used in turfgrass production in parts of Canada (Elkiey & Ormrod, 1980; Richards et al., 1980).

14.2.4 Mode of Action / Causal Mechanisms

The overall impact of ozone on vegetation is a function of the net effect of both toxifying and detoxifying mechanisms present. Plant responses to ozone exposure begin at the leaf surface. Ozone can be destroyed at the leaf surface through interactions with surface waxes. Oxidation or cleavage of surface waxes can lead to changes in composition and physical properties of the leaf surface (e.g. decreased water repellence) that may subsequently affect the uptake of ozone. Once ozone enters the leaf via open stomata, it has the potential to impair cellular function. One response to the presence of ozone within the stomatal space, is a reduction in stomatal conductance reducing subsequent ozone impacts during that exposure period. The mechanism is not well understood, but it has been shown in one study to be related to histological changes in guard cells and resultant loss of stomatal control. More research is needed in this area, however, as some evidence also exists that under certain conditions, ozone may cause stomatal opening.

Once inside the intercellular air spaces and mesophyll, ozone is thought to persist primarily as O_3, although superoxide anions and hydroxyl radicals are also formed to a lesser degree. These oxidants may react with cellular components, as well as major cell-wall constituents such as cellulose, lignin and pectins. Because these oxidants are also produced within the cell as a result of normal photosynthetic processes, and are injurious to cell constituents, plants have evolved enzymatic mechanisms to transform oxidants to less toxic forms. The detoxifying enzymes are saturable, thus cellular systems may be overwhelmed by the presence of extra oxidants from ambient ozone exposure, resulting in plant damage.

These exclusion or detoxifying mechanisms reduce the amount of ozone that can react with photosynthetic and respiratory components. Their role in determining ozone sensitivity among species or cultivars is not well understood, as there is not at present a conceptual model describing plant resistance to oxidants. Scientific understanding of resistance remains uncertain. It seems clear that the detoxification of ozone and its products would consume energy, although whether this additional energy burden would significantly decrease plant productivity, relative to the direct effects of ozone on photosynthesis for example, is not known.

Once inside the leaf, ozone can affect a variety of individual cellular processes. Biochemical impacts of ozone have been observed in:

1. chloroplast metabolism;
2. photorespiration and respiration;
3. carbohydrate metabolism;
4. nitrogen metabolism;
5. organic acids and lipids composition; and
6. secondary metabolism.

The major physiological processes affected by these biochemical changes are reductions in photosynthetic capacity and increased leaf senescence. Reductions in photosynthetic capacity have the potential to adversely affect carbohydrate allocation, growth patterns, leaf repair and overall growth and reproductive capacity. One of the major impacts of altered carbohydrate allocation is on the availability of carbohydrate resources to the roots and associated mycorrhizal fungi. Reduced allocation of resources to root systems will occur as the plant tries to meet the needs of foliar repair and/or replacement resulting from ozone stress. Ozone induced changes in canopy density, root/shoot ratios and stem growth may also render plants more susceptible to other stresses.

In summary, it is the integrated cellular system that confers and determines plant sensitivity to ozone (Runeckles & Chevone, 1992). That is, plant responses that result in visible changes are secondary responses to ozone toxicity, which appear after initial defence mechanisms are overrun. Biochemical and physiological changes can occur without visible injury symptoms appearing.

14.2.5 Uncertainties

Threshold versus Non-threshold Response

An absolute threshold ozone concentration above or below which vegetation injury will or will not occur has not been identified in the scientific literature. A threshold exposure level for plant biochemical response to ozone is largely conceptual in nature. Theoretically, biochemical systems could reach a saturation level above which they can no longer compensate for injury caused by ozone. A threshold dose response for ozone may exist, but the threshold may be so subtle that it cannot be detected, given current methods of investigation.

The form of some ozone exposure indices suggests that a threshold does exist, although there is currently no scientific justification for identifying a threshold. For example, the AOT40 index is calculated by summing hourly ozone concentrations greater than 40 ppb (censored). The forty ppb level was selected based on the notion that natural sources of ozone precursors will result in a 'background' ozone level. It is assumed that ozone concentrations greater than 40 ppb occur due to emissions of anthropogenic precursors. The SUM60 index is calculated by summing hourly ozone when concentrations are equal to and above 60 ppb. This exposure index has performed well in relating yield loss with ozone exposure using NCLAN data. However, there is no biological basis for inferring that hourly average concentrations below 60 ppb are not important in affecting vegetation. Sigmoidal-type indices, such as the W126 index, reflect that the magnitude of the plant response may be dependent on ozone concentration, but that a response occurs at all concentrations.

Modeling Ozone Exposure and Plant Response

The ozone-vegetation response literature has focused on the development of mathematical models of ozone exposure-response that best explain overall plant response to ozone. The statistical fit of the models are used to judge the suitability of a given exposure index.

There are limitations associated with using current ozone exposure - plant response models. For example, profiles of ambient ozone concentrations vary in space (altitude and latitude) and in time (year, season, month, hour) (Finlayson-Pitts & Pitts, 1986; U.S. EPA, 1986; Multistakeholder NO_x/VOC Science Program, 1997). Similarly, biological diversity and function are also highly variable in space and time since they are regulated by the variability in abiotic and biotic factors. These relationships underscore the uncertainty in current ozone exposure-vegetation response models.

The research community recognizes the need to mimic field conditions as closely as possible in air quality impact studies. This prompted development of open top chambers (OTC). OTCs are useful in assessing ambient ozone effects on crops using comparisons between charcoal filtered (CF) and non-filtered (NF) air, as long as sufficient numbers of replicate chambers are used to provide adequate power to the statistical analysis (Rawlings et al., 1988). The charcoal filter removes ozone from the input air to obtain a specified ozone concentration and therefore CF plots act as control plots. NF plots have ozone concentrations close to ambient air concentrations. In addition, ozone can be added to NF plots in order to study plant responses to elevated ozone concentrations. However, problems may develop when comparisons are made among the charcoal filtered, non-filtered and ambient air treatments. Systematic investigation of potential chamber effects on plant responses is required. Chamber effects may arise as a result of changes to various aspects of the environment within the OTC (e.g. moisture, chemical composition, light). Therefore, OTC experiments represent a large step towards mimicking field conditions, but do have limitations. Lefohn et al. (1989) have discussed the lack of similarity between some open-top chamber artificial ozone exposure experiments (e.g. NCLAN) and ambient ozone exposures.

Chamberless field experiments do have some advantages over OTC experiments; however, accurate determination of ozone concentrations at the plant remains a challenge. Ideally, experimental data should support apportioning the contribution of ozone, relative to the contributions of other variables (e.g., other air pollutants, temperature, precipitation, biotic diseases, etc.), to the overall observed or predicted effect.

Assessing the Effects of Ozone on Managed and Un-Managed Tree Species

Trees are long-lived perennial plants that are exposed to ozone repeatedly during the year over many years. Adverse effects of ozone on seedlings or young trees can be evaluated under experimental conditions; however, the large size of trees at maturity represents a challenge for either chamber or chamberless fumigations. This has limited the assessment of ozone impacts to visual observations of foliar injury, and changes to radial and height growth of individual trees within stands. Where analysis of tree growth is undertaken in different forest stands, selected on the basis of air quality gradients, the data must then also be considered in terms of edaphic and climatic site variation. Another complicating factor is the process of inter- and intra-plant species competition and possible alterations in successional processes and species composition. In this regard, an adverse effect on the growth or survival of one tree species could have either a beneficial or detrimental effect on the growth or survival of another species, thereby increasing or decreasing the total productivity of a mixed forest stand. In some instances, researchers have been able to attribute growth reductions to ozone specifically, among other factors that may have influenced tree growth (McLaughlin and Downing, 1996). In general, however, definitive conclusions concerning the role of ozone in recorded growth reductions are still not possible due to the difficulty involved in experimental resolution and in partitioning these effects from other variables that also affect tree growth.

Reference Point From Which to Assess Impacts

A key issue in modeling ozone exposure and crop response is to identify what the control concentration or reference point should be for comparison with experimental ozone exposures or ambient exposures. For example, the U.S. NCLAN, used a seven-hour seasonal average ozone concentration of ~0.025 ppm as the reference point, below which it was assumed ozone impacts would naturally occur. Heuss (1982) and Lefohn et al. (1989, 1990) have questioned this level because they contend that, in many rural areas of the U.S. and even in the so-called "pristine" areas of the world, average hourly ozone concentrations frequently exceed this level during the growing season. Altshuller (1987), to the contrary, provided some support for the NCLAN reference point of 0.025 ppm. If the control or reference concentrations used in the experimental design are below “background” levels, then the resulting losses associated with higher ozone exposures may be overestimated.

14.2.6 Co-Occurring Pollutants

The interaction of ozone and nitrogen oxides or the three- or four-way interaction of ozone, sulphur dioxide, nitrogen oxide and acid rain has not been specifically addressed in any of the field oriented, crop yield response research to date. Although photochemical smog and other forms of atmospheric pollution involve numerous pollutants in addition to ozone, the limited amount of information available on their combined effects on vegetation precludes any specific estimate of the magnitude of these effects in relation to the effects of ozone alone. This finding should be considered in the light of information published by Lefohn and Tingey (1984) and Lefohn et al. (1987) on patterns of co-occurrence of ozone, SO_2, and NO_2 in urban, rural and remote sites in the U.S. during 1978-82, which found that co-occurrences were usually infrequent and of short duration. They also reported that the most frequent types of co-occurrence were usually sequential or a combination of sequential and overlapping exposures of short duration.

Because of its phytotoxic potential, peroxyacetylnitrate (PAN) could be the most relevant co-occurring pollutant and would not be expected to exhibit short-duration type of co-occurrence. Although PAN has been documented as acting synergistically with ozone in causing increased foliar injury to some species under some conditions, this combined impact cannot yet be generalized, as considerable variability has been demonstrated in the experimental findings published to date (synergistic, antagonistic and additive responses). Given the relatively low levels of PAN reported in the Canadian atmosphere, there is no compelling evidence for consideration of combined impacts with PAN in this review; however, it is a potential area of interest for research in the future. The most recent studies involving ozone interactions with other atmospheric components include the effect of carbon dioxide (climate change) and ultraviolet light (resulting from stratospheric ozone depletion) are preliminary and considered inconclusive.

14.2.7 Weight of Evidence

No other phytotoxic air pollutant has been studied as intensively as ozone. From the date of its first causal linkage with crop damage in the U.S. in 1958 to the present time, there have been literally thousands of concentration-response studies conducted throughout North America, Europe, Australia and numerous other countries. Based on a plethora of scientific evidence, it is now universally accepted that ozone is the most damaging of all air pollutants affecting vegetation, with many regions worldwide experiencing sufficiently high ozone levels to impair the growth and yield of sensitive plants. Certain agricultural crop species are continually observed to be more susceptible to ozone, regardless of where they are grown. Visible foliar injury has been observed in crops grown in British Columbia, Ontario, Québec and New Brunswick, providing empirical evidence that crops are being affected at ozone concentrations currently experienced in Canada.

More recently, there has been significant attention directed to the study and assessment of ozone impacts on vegetation with the intent of developing air quality criteria (e.g. in the U.S., Europe and Canada). Based on these activities, the following conclusions can be made concerning the weight of evidence behind the current state of knowledge.

- The toxicological evidence for ozone impacts provides a plausible mechanism for effect, though there remain areas that are poorly understood (for example, the mechanism of response of stomatal conductance to the presence of ozone). However, there is no significant debate over the general toxicological mechanisms of ozone impact.
- The research community is comfortable with the use of a cumulative exposure index to relate ambient ozone air quality to yield or biomass losses for both agricultural crops and forest species.
- The selection of the most appropriate cumulative exposure index to use (e.g., SUM60, AOT40 etc.) appears to be a decision which requires a subjective interpretation of the available science, accommodation of existing uncertainties in the experimental databases, and awareness of the forum in which such indices will be applied. In this regard, there appears to be significant comfort among expert panels in North America with selection of the SUM60 index.

Overall, the best experimental databases currently available are the OTC studies of NCLAN and EOTCP, which provided a basis for developing statistical relationships between agricultural crop yield losses and ambient ozone concentrations. The NCLAN study utilized study locations across the continental U.S. and yield loss results are of similar magnitude within the NCLAN study and the EOTCP study. Short-term foliar injury has been linked with high ozone levels experienced within 24 hours prior to the impacts being observed. It is more difficult to determine the sole specificity of ozone over longer time periods where the chronic effect may be influenced by environmental / meteorological parameters. The statistical relationships observed between ozone concentrations and yield loss in the OTC programs are weak given the limited sample sizes (i.e., number of crops and cultivars tested) and opportunity for replication. However, the yield response is consistent with that expected from the toxicological understanding of ozone impacts. Given that these OTC experiments restrict the composition of the input air, it is possible to screen out other potentially confounding air pollutants. It can be stated with reasonable confidence that the observed yield losses are due to ozone impacts.

In spite of the scientific consensus regarding the impact of ozone on plants, there continues to be active research on a number of outstanding scientific issues. These can be summarized as follows:

1. The majority of the plant response literature, particularly those studies conducted prior to the design of the open-top chamber field exposure system in the early 1970s consisted of short-term, acute fumigations and assessment of foliar injury response under greenhouse or controlled-environment chamber conditions. However, it is now known that these types of exposure may not adequately characterize the season-long, chronic effects of ozone exposure on crop and forest yield or biomass production. What is needed is the development of experimental protocols designed to assess the impacts of season-long exposures to realistic concentrations of ozone.
2. Even the best designed experimental exposure systems, intended to mimic natural growing conditions, may modify plant response. Experiments designed to evaluate the extent to which the experimental system itself is a factor in the response of plants to ozone (and other air pollutants) are required.

3. There has been renewed interest in the concept of "exposure dose" versus "effective dose", as researchers attempt to understand ozone exposure-plant response relationships under conditions that simulate as closely as possible the dynamics of season-long ozone profiles and plant growth. The term effective dose may be defined as the actual concentration absorbed by the plant over time, whereas the exposure dose is simply the air concentration and exposure duration to which the plant is subjected. What is required is an appropriate exposure index for use in impact assessment that most closely approximates the effective dose. Some of the related issues include:
    - the biological relevance of plant response data generated by using enhanced ozone treatments in OTC conditions, and the potential for enhanced sensitivity of plants to ozone;
    - the relative importance of peak versus mid-range ozone concentrations, and of exposure duration versus concentration, in eliciting plant responses over season-long exposures;
    - the cumulative effect of ozone uptake into plant foliage, and the importance of exposure episodicity and plant respite time during which metabolic detoxification can occur; and
    - the importance of plant phenology considerations and the timing of ozone exposure in the expression of ozone exposure-plant response.
4. The need for improved ambient air quality monitoring networks that will provide information on the exposure of plants in rural and forested areas to ozone and on ozone concentrations at the plant surface boundary layer. Specifically, the majority of ozone monitoring remains in populated urban centres where scavenging of ozone is known to alter the concentration and frequency profile of ozone.

Many of the foregoing issues are of greater importance to the development of predictive capabilities for risk estimation purposes and in the development of air quality objectives/standards than for the establishment of Reference Levels. The need to better understand plant exposure – response relationships does not, however, alter the finding that the weight of evidence supports the conclusion that ozone is a probable and likely cause of agricultural crop and forest impacts, ranging from acute foliar injury symptoms to chronic yield and biomass losses. That the information base is sufficient for such a conclusion is the collective opinion of vegetation experts (Heck and Cowling, 1997; Heck et al., 1998). However, in order to estimate the magnitude of impacts across Canada at current ambient ozone concentrations, additional information on rural ozone concentrations would be required.

14.2.8 Recommendations

Based upon the weight of evidence discussion, ozone is a probable and likely cause of agricultural crop and forest impacts ranging from acute foliar injury symptoms to chronic yield and biomass losses. Therefore, there is a risk to vegetation (including agricultural crops, forest species and horticultural species) at ambient ozone concentrations currently experienced in Canadian urban and rural areas. Quantification of that risk for Canadian species is currently constrained by the lack of information on exposures in non-urban areas (i.e. rural ambient ozone data).

Recommendations for improving the scientific understanding of ozone impacts on vegetation have been summarized in section 8.4 and discussed also in the previous section (14.2.7). Most limiting is the dearth of information on experimental exposures of Canadian agricultural and forest species, grown under Canadian field conditions, at realistic (i.e. near ambient) ozone levels. The analyses in this assessment are to a large extent based upon experimental data collected in the United States and Europe. While the theoretical understanding of ozone vegetation impacts and ambient characteristics of ozone in Canada support the use of this information, it is important that experimental work be carried out to assess exposure – response relationships for Canadian crops and forest species under Canadian climatic and pollutant conditions. In the meantime, it is recommended that when species specific response information is required, the individual LOAELs, presented in Tables 8.9 and 8.11 for agricultural crops and forest species respectively, be used. For a conservative estimate of the concentration of ozone above which effects on vegetation can be expected, the LOAEL ranges of 5900-7400 ppb-h (crops) and 4,400-6,600 ppb-h (trees) (3 month SUM60 values) identified in Section 8.2.3 (and again in section 13.2.3) should be used.

14.3 EFFECTS ON BIRDS AND MAMMALS

14.3.1 Effects Summary

For both birds and mammals, the only significant exposure route is inhalation. Therefore, as is the case with humans, the effects of concern have to do with impacts on the respiratory system. There are notable differences, however, between the lung-air sac respiratory system of avian species and the mammalian bronchoalveolar lung. Among the most important of these are that birds have a higher mass-specific minute ventilation, higher mass specific effective ventilation of gas-exchange tissues, cross-current and counter-current gas-exchange mechanisms and a gas diffusion barrier half the thickness of that of mammals (Brown et al., 1997). While these differences may predispose birds to greater sensitivity to inhaled toxicants, there is insufficient information at present to make any predictions concerning relative sensitivities. There appears to be a complex relationship between a species' respiratory physiology, its pathophysiologic response to a toxic gas and other physiologic factors.

Effects on Birds

Very little information on the effect of ozone on birds and wildlife is available. Only three studies were found that reported on effects on birds, and all of these involved domesticated birds and their response to acute exposures. Lung haemorrhage was noted in all three studies, and therefore this appears to be a consistent effect in birds in response to exposure to ozone. The absence of data on potential effects of chronic exposures is clearly a weakness of the current database. However, the observed damage to the lungs and some evidence that birds may lack the biochemical / morphological repair mechanisms observed in mammals, raises concern that birds may be particularly susceptible to respiratory effects from chronic exposure to ozone. The lack of information on wild birds is also of concern since studies on domestic birds did not involve flight which would put additional demands on a damaged respiratory system.

Effects on Mammals

Eleven studies were reviewed, all on domestic mammals. Most of these studies were on sheep, because sheep have been proposed as a potential animal model for human effects. One study examined developmental effects, three examined effects on red blood cells, and seven investigated inflammatory responses. All of these studies involved acute exposures. No studies were found that dealt with chronic exposures. The most consistently observed responses included adverse effects on red blood cells and inflammatory responses (e.g. increases in the number of mast cells and lymphocytes in airways, increases in airway permeability and responsiveness etc.). Developmental effects (retarded development of the tracheal epithelium) were noted in the one study on lambs that examined this endpoint. However, high experimental concentrations were used (the investigators used 1 ppm ozone for 4 hours per day for 5 days) and therefore the relevance of this work to understanding the effects of ambient exposure is questionable.

14.3.2 Concentration-response Relationships

There was insufficient information to develop concentration-response relationships and very limited information on which to base effect levels. Based on the information provided in Chapter 9, lung haemorrhage was seen in chickens exposed to 0.3 ppm ozone (300 ppb) continuously for periods of up to 1-3 weeks, and in Japanese quails exposed to 0.50 ppm ozone (500 ppb) continuously for 1 week. Japanese quails exposed to 0.15 ppm ozone (150 ppb) did not show this effect and therefore, for this study, 0.15 ppm ozone can be identified as a NOAEL for lung haemorrhage. However, given the paucity of experimental data and the lack of experimental exposures that reflect ambient conditions, no other more general conclusions can be drawn about possible effect levels in birds.

For mammals, statistically significant effects on red blood cell counts were noted at 0.25 ppm (250 ppb) ozone, but not at 0.12 ppm (120 ppb) (exposures lasting 2.75 hrs.), although it should be noted that some evidence of oxidative stress was observed at the 0.12 ppm level. Red blood cell effects appear to be the most sensitive endpoint for assessment of effects of ozone on mammals based on the evidence presented. However, studies that examined inflammatory responses following exposure to ozone tended to use higher exposures. The lowest experimental exposure was to 0.5 ppm ozone (500 ppb) for varying periods of time and effects were noted at this level. Given the paucity of experimental data and the lack of experimental exposures that reflect ambient conditions, no other more general conclusions can be drawn about possible effect levels in mammals.

14.3.3 Susceptible Species

Insufficient information is available to identify species of birds or mammals particularly at risk from exposure to ozone. As a group, birds have been identified as possibly being vulnerable to the effects of ozone. This concern arises as a result of the peculiarities of the avian lung-air sac respiratory system, the demands put on that system during flight and the apparent lack of, or at least uncertainty surrounding, the effectiveness of molecular repair mechanisms in birds.

14.3.4 Mode of action / Causal Mechanism

Ozone's biological effect is attributed to its ability to cause oxidation or peroxidation of biomolecules directly and/or via free radical reactions. A sequence of events may include lipid peroxidation and loss of functional groups of enzymes, alteration of membrane permeability, and cell injury or even death (Mustafa, 1990).

14.3.5 Recommendations

The lack of suitable dose-response information precludes any quantitative analysis of the risks to birds and mammals across Canada from exposure to ozone at current ambient concentrations.

14.4 HUMAN HEALTH

The health effects of ozone have been examined in human epidemiological studies, controlled human exposure studies, and animal toxicology studies.

14.4.1 Effects Summary

Epidemiological studies

Epidemiological studies have demonstrated convincing evidence for the association of ozone (and other co-occurring pollutants) with mortality and morbidity.

Mortality studies indicate that the association between ozone and non-accidental mortality was positive and consistent in cities across North America, in Santiago Chile and in Europe. The association was found at mean ozone concentrations (one-hour maximum) between 20 and 75 ppb, despite widely varying climatic conditions and pollutant mixtures in the study locations. Bivariate and multivariate regression analyses also show that ozone effect was independent of other co-occurring air pollutants including particulate matter. The average mortality risk due to ozone in single pollutant analysis was 0.4% (95% CI: 0.19-0.60%) per 10 ppb increase in ozone (1-h max), based on a meta-analysis combining the data from 10 studies with adjustments for seasonal cycles, weather terms, and co-pollutants. Several studies indicate that ozone concentration-response curves were approximately linear, down to less than 10 ppb without evidence of any threshold at low concentrations. Only a few studies provided evidence of a more specific cause of death; cardiovascular deaths were associated with ozone increases in several studies while respiratory deaths were not, possibly because of proportionally fewer deaths in the latter category.

The weight of evidence is strong for an association between hospitalizations for respiratory conditions and exposure to ozone at the levels now commonly encountered in Canada. Estimates of risk per 10 ppb increase in ozone (1-hour maximum) range from 1.14% (95% CI 0.43-1.84%) to 1.9% (95% CI 1.2-2.6%) based on meta-analyses of data from single pollutant models (Thurston and Ito, 1999). Meta-analysis of data from multi-pollutant models reached a similar result; the weighted mean for respiratory hospitalizations per 10 ppb increase in ozone (1-hour maximum) is 1.12% (95% CI 0.73-1.51%). These studies included all of Southern Ontario, 16 cities in a cross-Canada study, and eight U.S. cities. The ozone-associated increases in respiratory hospitalization occurred in places where the mean concentrations are well below the current Canadian objective of 82 ppb. The 95th percentile for ozone in the 16 cities of the national Canadian study was only 60 ppb.

The data on hospital Emergency Department (ED) visits generally support the findings from the respiratory hospitalization studies, i.e., increases in ambient ozone concentrations are associated with significantly increased visits to the Emergency Department. The percent increase in respiratory ED visits was 6-8.6% per 10 ppb ozone (1-hour maximum), and was 5.6-14.2% per 10 ppb ozone (5-hour average) after adjusting for PM, temperature, and other gaseous pollutants. The associations were seen in four cities/metro areas in three different countries, at mean summertime ozone levels (1-5 h metrics) that varied between 30 and 90 ppb.

It should be specifically pointed out that the results from the most recent reanalysis of a large Canadian database by Burnett (1998, details in Appendix A) demonstrate a strong consistency with the previous mortality and hospitalization studies. This study, encompassing 13 Canadian cities, was carried out in response to a request from the WGAQOG. The respiratory hospitalization data were from two Canadian studies (Burnett et al., 1994, 1997a). The mortality data were also obtained from the same cities. The regression analysis shows that the risk for non-accidental mortality was 0.79% (95% CI: 0.59-0.99%) for every 10 ppb increase in ozone (daily 1-hour maximum). The results also demonstrate that the ozone risk associated with hospitalization for respiratory diseases was 1.04% (95%CI: 0.78-1.30%) per 10 ppb increase in ozone (daily 1-hour maximum). Since previous studies using a similar database have shown that carbon monoxide, nitrogen dioxide and sulphur dioxide did not confound ozone effects on mortality (Burnett et al., 1998) or on respiratory hospitalization (Burnett et al., 1994), and particulate sulphates did not confound the ozone effect on hospitalization (Burnett et al., 1994, 1997b) (no mortality data), it is reasonable to assume that the ozone effects demonstrated by Burnett (1998) are independent of other air pollutants.

The advantage of this study (Burnett, 1998) is that it provided an estimate of the lowest observed adverse effect level (LOAEL) of ozone with statistical significance for both mortality and hospitalization. The LOAEL for non-accidental mortality was 20 ppb (1-hr maximum)

($p<0.01$). The data continue to show a trend of positive association with ozone values as low as 10 ppb. There appears to be no threshold for mortality. The LOAEL derived from the respiratory hospitalization data with statistical significance is 25 ppb (1-hr maximum) ($p<0.01$). Interestingly, the regression coefficient data show a potential threshold at between 15 and 20 ppb of ozone (daily 1-hour maximum) for respiratory hospitalization.

The field (camp and panel) studies show that exposure of healthy and asthmatic children and adults to ozone under ambient conditions can result in measurable declines in lung function and increases in symptoms and asthma medication use. Outside workers and individuals who are exercising out of doors in summer experience measurable declines in pulmonary function, and, if exposures are repeated on consecutive days, possibly also a systematic decline in pulmonary function. The concentrations of ozone encountered in the field studies with significant health effects were as low as 40 ppb. Asthmatics should be considered as a vulnerable population in this context, as their airway responsiveness is already increased, and their lung function may be lower than in the normal population.

Chronic effects have been more difficult to demonstrate because of the technical difficulty of conducting appropriate epidemiological studies and a consequent dearth of data. In areas with chronically high ozone levels, a worsening of asthma symptoms, increased bronchial hyperresponsiveness and altered immunological function and lung function have been observed in the few studies available. New evidence published in 1996 and 1997 for persistent decrements of small airway function and new cases of asthma from chronic ozone exposure suggest that long term exposure to ambient ozone could be a significant concern (Nushino et al., 1996; Kunzli et al., 1997). A common drawback of the chronic effect studies is the lack of evaluation of other co-occurring pollutants.

Controlled human exposure studies

An important finding of human clinical studies is that at a given ozone concentration and exposure duration, the increase in ventilation results in elevated pulmonary function responses and inflammation. An increase in ventilation rate also lowers the concentration of ozone required for a given pulmonary response. Thus the concept of "effective dose" is introduced, namely, a product of the minute ventilation rate ($\underline{V}_E$), the concentration of ozone ([ozone]) and the exposure duration ($\underline{V}_E$ x [ozone] x duration). This concept allows us to further establish models and to investigate the sensitivity of people with different ages, genders, disease status and exercises in response to ozone exposure.

Exposure to O_3 under controlled conditions leads to the appearance of symptoms (cough, shortness of breath, etc.), decrements in spirometric values, increases in airway resistance and bronchial responsiveness to stimuli, and airway inflammation. There is a large variability in response to O_3 exposure between individuals. The range of response within each individual also varies, albeit not as much as between individuals. Prolonged exposure (6 to 7 hours) of healthy subjects to ambient levels of ozone (0.08 to 0.12 ppm) with intermittent exercise at ventilation rates ($\underline{V}_E$) of 35 to 50 L/min may cause increased bronchial responsiveness to methacholine, increased inflammation in deep airways, and decreased FEV_1. For shorter exposure duration (1 to 4-hours) to 0.12 ppm ozone, a significant increase in bronchial responsiveness has been observed, while little or no change in pulmonary function is seen. No data have been reported on inflammatory response for the shorter exposure periods.

A study using varying doses (0 to 240 ppb, back to 0 ppb) as well as a constant dose of 120 ppb over 8 hours has demonstrated that the varying doses produced FEV_1 decrements almost twice as much as the constant dose of ozone, although the total concentration was the same in the two dose regimens (Hazucha et al., 1992). These results suggest that the average dose value calculated as a mean over an 8-hour exposure may underestimate the effect of ozone on pulmonary function induced by a peak exposure.

A limited number of clinical studies have investigated the age difference in response to ozone. It appears that adolescents are more sensitive to ozone-induced pulmonary function decrements when compared with adults using the same dose regimen. However, older adults (60 years or older) have not been demonstrated to be more susceptible to ozone-induced pulmonary function changes than their younger counterparts when given the same dose. No study has been done on age differences in inflammatory responses. Therefore at present, based on limited studies, age does not appear to be a major determinant of response to ozone exposure. More research is needed, however, to elucidate this aspect of the issue.

People with pre-existing respiratory diseases have been demonstrated to be more sensitive to ozone-induced health effects than are healthy individuals. Patients with chronic obstructive pulmonary diseases (COPD) had significantly greater loss of FEV_1 than their same age healthy counterparts (-19% versus -2%, respectively). when exposed to 0.24 ppm ozone for 4-hours during intermittent exercise ($\underline{V}_E = 20$ L/min). COPD patients also showed moderate increases in symptoms and decrease in blood oxygenation, conditions which were not seen in healthy subjects.

For patients with asthma, prolonged exposure (6 to 8-hours) to 0.12 to 0.16 ppm ozone ($\underline{V}_E$ approximately 30 L/min) has demonstrated more pronounced decrements of FEV_1 in asthmatics than in healthy subjects. Moreover, asthmatic subjects are revealed to be more sensitive toward ozone-induced airway inflammation than healthy subjects. At concentrations of 0.12 to 0.24 ppm (90 minutes at $\underline{V}_E \cong 50$ L/min, and 6-hours at $\underline{V}_E \cong$• 25 L/min), ozone induced greater inflammatory responses in asthmatics than in healthy subjects. For patients with allergic rhinitis, data suggest that they have a greater rise in airway resistance than healthy subjects when exposed to 0.18 to 0.25 ppm ozone for 2 to 3-hours with intermittent exercise ($\underline{V}_E \cong$• 30 L/min). Allergen treatment exacerbated ozone-induced FEV_1 decrements in these patients.

To date, no cardiac patients have been tested for their susceptibility to ozone exposure. No clinical studies on lung injury using ozone concentrations lower than 80 ppb have been reported.

Animal studies

Collectively, in the animal studies, the deposition modelling of inhaled ozone indicates the terminal bronchiolar and centriacinar regions as sites of maximal tissue deposition of the gas. The principal effects observed after acute exposures of a variety of species to ozone concentrations less than 1.0 ppm, are lung inflammation and changes in lung permeability; increased airway responsiveness; and increased mortality if the animal was subsequently challenged with a bacterial aerosol. Reactive oxygen intermediates are involved in ozone-induced cell damage.

In most of the animal studies, the doses used are higher than those used for human clinical studies, as well as those seen in ambient air. However, a recent comparative dosimetric study has provided some very interesting and valuable data in this respect. Hatch et al. (1994), using humans and rats exposed to ^{18}O-labelled ozone, were able to demonstrate that exercising humans had 4- to 5-fold higher ^{18}O concentrations in all of their bronchioalveolar lavage constituents than did the resting rats, when they were acutely exposed to the same dose of ozone (400 ppb). The humans also had significant increases in all of the airway inflammatory markers after 400 ppb ozone, whereas the rats did not. Thus, it is conceivable that the doses used in rats (as low as 100 ppb) that produced pathological changes are rather relevant to the concentrations encountered by human populations during ozone episodes.

When ozone is delivered into deep airways, the relationship between the pulmonary tissue dose (normalized to body weight) and the pulmonary injury (measured as bronchoalveolar lavage protein) is estimated to be in the same linear pattern among rats, guinea pigs, rabbits and humans (US EPA, 1996). This prediction is supported by the study of Hatch et al. (1994), showing that rats exposed to 2000 ppb ^{18}O-labelled ozone had levels of ^{18}O and the inflammatory markers in bronchoalveolar lavage more comparable to those in humans who were exposed to 400 ppb ^{18}O-labelled ozone. In rats, 49.6% of ^{18}O-labelled ozone was taken up by the head, 6.7% by the larynx/trachea, and 43.6% by the lungs (Hatch et al., 1989).

These studies provide a valuable tool that should assist in extrapolating animal toxicity data to humans.

14.4.2 Exposure Assessment

Exposure is defined as any contact at a boundary between a person and a specific ozone concentration for a specified time interval. Exposure assessment involves estimating the intensity, frequency, and duration of human contact with ozone.

Direct personal monitoring studies have been conducted in an attempt to delineate the ozone exposure levels in the immediate microenvironment (breathing zone) of the person, as opposed to using data from a fixed ambient monitor (FAM). Personal monitoring studies for ozone in Canada (Brauer and Brook, 1995, Liu et al., 1995) and in the US (Liu et al., 1993) have demonstrated that mean personal exposures follow the same temporal trend as the FAM concentrations. Personal exposure data are highly correlated with ozone data from FAMs. These results suggest that ozone data from FAMs, often used in epidemiological studies, can be a good indicator for population exposure, especially during summer in Canada.

On average, ozone concentrations obtained from personal monitoring studies are 70% higher than those in indoor air, and 50% lower than those in outdoor air, and approximately 50% lower than the concentrations from FAMs. The drawback of most personal monitoring data is that the data are collected over relatively long averaging times (12 hours, 24 hours or weekly), and do not capture the peak value of ozone. Data from epidemiological studies have demonstrated that acute increases in mortality and morbidity are significantly associated with 1-hour maximum ozone concentrations. Averaging concentrations from longer terms cannot assess hourly exposures, but may be used for chronic effect studies.

Predictive exposure assessment studies using the probabilistic National (Ambient Air Quality Standard) Exposure Model (pNEM) provides estimates of the distribution of ozone exposures within a defined population for a specified exposure period. This model uses detailed information on human activity patterns, indoor-outdoor ozone ratios, and air exchange rates to predict how many days a "typical person" in a sub-population cohort will be exposed above any given level during a specified exposure period.

Results from pNEM modelling using populations from Toronto, Montréal and Vancouver in 1988, 1990 and 1991 demonstrate that an average of 42% (Vancouver) to 91% (Toronto) of the population was exposed to ozone above 82 ppb (1-hour maximum; the existing Canadian Air Quality Objective) at least once a year. Almost 92% to 100% of the population was exposed to 50 ppb or higher levels of ozone at least once a year. During the worst pollution year (1988), almost half of the Toronto population was exposed to 82 ppb ozone for more than 5 days, whereas in Vancouver only 6.4% of the population was exposed to 82 ppb ozone for more than 2 days. The pNEM data are in agreement with the results from FAMs indicating that the ambient ozone concentrations and the number of episode days are significantly higher in Toronto than in Vancouver, with Montréal in the middle of the range.

The pNEM data are also in line with Canadian hospitalization studies that have consistently shown a lower hospitalization risk associated with ozone in Vancouver and Montréal than in other parts of the country. The pNEM model was developed just recently, and data generated using pNEM have not been widely used for epidemiological studies.

14.4.3 Criteria for causality

The criteria first described by Hill (1965) and modified by succeeding epidemiologists are used in this document to provide some useful guidance for drawing an inference of causality from health effects data:

Strength of Association

The associations seen in all the epidemiological studies are in the range of 0.4% to 8.6% increase in mortality and morbidity endpoints for a 10 ppb increase in ozone (a relative risk of less than 1.50, or 50% increase in an endpoint, is considered to be low). They are, however, statistically significant in many cases. Although the magnitudes of these estimates of increased risks are seemingly small, they represent large numbers of people since most of the population is exposed, and would lead to significant effects on public health.

Consistency

Although the study designs of these time-series studies were similar, the association of ozone pollution with population health effects was seen by a number of investigators in various cities across North America and in several cities in central and South America, all of which differ in their pollutant mix, ozone levels, weather, and socioeconomic status. The 16 city Canadian study (Burnett et al., 1997a) included cities from all five regions of Canada. Only two were found to have marginally significant associations. The Ontario study by Burnett et al. (1994) was consistent with other studies that had taken place in the same geographic area (Bates & Sizto, 1987; Thurston et al., 1994a,b). Some studies for each endpoint were unable to find a positive association, but their negative results could usually be explained by the conduct of the analysis, such as lack of control for confounding factors, or small sample sizes.

Specificity

Air pollutants never occur in isolation, and ozone is always found in company with several other pollutants. The pollutant mix and the ratios of one pollutant to another differ according to location, season, time of day, and other factors. The majority of the authors reviewed in the epidemiological sections used some form of regression analysis, which is the best general method available for distinguishing between the effects of different pollutants that occur together on health endpoints. Several authors (Li & Roth, 1995; Kinney et al., 1995; Thurston and Kinney, 1995; and Cakmak et al., 1998) provided some comparison of the effects of various steps in several different regression models on the relationship of particulates, and other gaseous pollutants including ozone, to mortality. The type of regression, whether Poisson, Gaussian or other, did not make a substantial difference in the results. It is clear from the present review that the results identifying which pollutant(s) is responsible for a given health outcome, and at what concentration, are sensitive to several steps in the regression analysis.

A number of epidemiological studies indicated that ozone was the most important of the several pollutants in the mixture for hospitalizations, Emergency Department visits, and asthma attacks. The hypothesis that H^+ was an important component of the pollutant mixture and possibly had an effect on ozone, was tested in the study by Delfino et al. (1997) on Emergency Department visits in Montreal. H^+ was not associated with ED visits for any age group, except for infections in infants (Delfino et al. 1997). Recent data from environments in which aerosol acidity is known to be absent, and in which aerosol sulfates are at very low concentrations, serve to confirm that the primary association of health effects is with ozone (Brauer et al., 1996a,b).

Data obtained from controlled human exposure studies demonstrate that simultaneous exposure to mixtures of ozone (0.12 - 0.6 ppm) with SO_2, NO_2, H_2SO_4, HNO_3, or particulate aerosols for 1 or 2 hour, or with multiple combinations of these pollutants did not cause any significant interactive (additive or synergestive) effects for these chemicals. However, exposure to ozone (0.12 to 0.3 ppm) and co-pollutants including NO_2, sulphuric acid and SO_2, in sequential pattern, has shown an additive effect on bronchial responsiveness and spirometric parameters.

Temporality

Most authors of epidemiological studies investigated the possibility that pollutant levels one or more days before the hospital admission or ED visit (lag time) were more important predictors than current day concentrations. Lag times were generally 1 to 2 days for hospitalizations, and perhaps a little shorter for ED visits, especially if the hospital served as the only source of medical advice, as in areas of low socioeconomic status. In wealthier areas the family physician might be the first call. Negative lag times (health endpoints occurring before ozone changes) were investigated for both non-respiratory diseases and respiratory diseases by Thurston et al. (1994a,b), and Burnett et al. (1994), and were not found to be associated with the respiratory conditions, but were occasionally associated with other conditions by chance.

Concentration-response relationships

A concentration-response relationship for respiratory hospitalization and ambient ozone was clearly shown in the epidemiological study by Burnett et al. (1994) in southern Ontario and in 13 Canadian cities (Burnett, 1998). Data from the Canadian database (13 cities) (Burnett, 1998) demonstrate a risk of 1.04% increase in respiratory hospitalizations for each 10 ppb increase in daily one hour maximum ozone. Data from Canada, US, and European cities from single pollutant models, when pooled and weighted, show a 1.14-1.9% increase of respiratory hospitalizations due to 10 ppb increase in ozone (1-hour maximum). Using data from multi-pollutant models to control weather and co-pollutants, the weighted mean for respiratory hospitalizations per 10 ppb ozone (1-hour maximum) is 1.12%.

Population mortality analyses also demonstrate an ozone concentration-related increase in mortality (Burnett, 1998). Overall, the data show that the average mortality risk for a 10 ppb increase in ozone (1-hour maximum) was 0.4% (95% CI: 0.19-0.60%), after adjusting for seasonal and weather variations and co-pollutants. Using the data from the 13 Canadian cities (Burnett, 1998), the results show that the risk for non-accidental mortality is 0.79% for each 10 ppb increase in daily one-hour maximum ozone. The mortality data continue to show a trend of positive association with ozone values as low as 10 ppb. There appears to be no threshold for mortality. Lack of a demonstrated threshold may be interpreted to reflect the heterogeneity in responses among members of the population, some of whom might be considered more susceptible by reason of age, gender, activity level, and/or pre-existing disease condition.

One may argue that ozone concentration data from fixed ambient monitors (FAMs) used in epidemiological studies may not represent true human ozone exposure, since people spend most of their time indoors. However, personal monitoring studies conducted in Canada and in the US have demonstrated that mean personal exposures to ozone have the same temporal trend as the FAM concentrations, which supports that ozone data from FAMs can be a good indicator for population exposure. Ozone essentially is an outdoor pollutant and peaks during summer in Canada when people spend more time outdoors. This activity pattern is in line with the observations in epidemiological studies demonstrating increased ozone health effects in summer only (Burnett et al., 1997a). Based on Canadian monitoring data, of the 104 stations monitored across the country during 1986-1993, seventy percent had a median ozone concentration (1-hour maximum) exceeding 20 ppb, a concentration shown to be associated with non-accidental mortality (Burnett 1998, Appendix). In all of these stations, the 95th percentile ozone concentrations were above 20 ppb.

The concentration-dependent pattern of ozone effects is also supported by data from population exposure estimates using the probabilistic National Exposure Model (pNEM). The pNEM study demonstrated that when time-activity patterns and microenvironment ozone data were incorporated for population exposure estimates, Vancouver and Montréal had much lower population exposure levels for ozone than Toronto. This is in agreement with epidemiological observations that in Vancouver and Montréal, the risk of hospitalizations associated with ozone are lower than in other Canadian cities (Burnett et al., 1997a; Delfino et al. 1994).

Dose-response relationships have been demonstrated in controlled human exposure studies for a number of spirometric variables as well as some symptoms. There have been no models established for airway inflammation. For symptoms, the variability of responses, combined with the subjectivity of assessment of response and the differences in the response measurement schemes precludes the establishment of a good correlation that can be used as a predictive model. For some of the spirometric variables, significant correlations with ozone exposure were demonstrated and predictive models were developed. The dose-response curves derived from models have shown that the response varies with the "effective dose" (i.e. the dose that reflects O_3 uptake which varies with $\underline{V}_E$, exposure duration, and ozone concentration). Based on the "effective dose", there appears not to exist a threshold for ozone-induced spirometric responses. Although studies using FEV_1 as an indicator have shown a LOAEL of 80 ppb (2 hours exposure, with intermittent exercise at $\underline{V}_E$ >40 L/min) for healthy subjects, a longer exposure period or higher $\underline{V}_E$ (such as in the case of an athlete performing vigorous exercise) at concentrations below 80 ppb might still cause an adverse health effect. Since airway inflammation markers appear to be more sensitive indicators of ozone effects than lung function, it is possible that a LOAEL for tissue injury would be even lower. It must be kept in mind that no clinical data have been reported at exposure levels below 80 ppb.

Biological Plausibility

Ozone has been shown in animal experiments and in human controlled exposure studies to result in inflammation, cell necrosis, lowered lung function, increased airway reactivity, and increased animal mortality when the animals were subsequently challenged with a bacterial aerosol. In addition, asthmatics and individuals with 'hyperreactive' bronchi have been shown to be sensitive to the effects of ozone, with pain on deep inspiration, lowered lung function, increased need for medication, and asthma attacks. The progression of these effects to the point where medical attention is sought is quite plausible in light of the above. Reactive oxygen intermediates are believed to be involved in ozone-induced cell damage, which is partly caused by auto-oxidation chain reactions.

It is true that the doses used for animals (above 100 ppb) that produced pathological changes are higher than those seen in ambient air. However, considering that humans receive 4 – 5 times more ozone in their lower airways than rats do when given the same exposure dose (Hatch et al., 1994), it is conceivable that the doses used in rats are rather relevant to the concentrations encountered by human population during ozone episodes. Furthermore, once ozone is delivered into lower airways, the relationship between the pulmonary tissue dose (normalized to body weight) and the pulmonary injury has been predicted to be similar (same linear pattern) among rats, guinea pigs, rabbits and humans (US EPA, 1996).

Coherence

The data from the three administrative databases on mortality, hospitalizations, and emergency department visits provide quite a coherent picture of progression of effects, from high numbers of incidents recorded as ED visits to lower numbers for those who were hospitalized. For a given ozone concentration, the percentage increase in ED visit (6-8.6% per 10 ppb) was larger than the percentage increase in hospitalizations (1-2% per 10 ppb). This difference should be expected on the basis that an element of choice is involved in the decision to seek medical attention at an Emergency Department or doctor's office, while hospitalizations represent only the most serious cases as determined by a physician.

At first glance, there seems to be a lack of coherence when one moves from respiratory hospitalizations to respiratory mortality, since the percent increase in mortality was so low as to cast some doubt on whether the effect was real. This may be partly explainable on the basis that respiratory mortality is a small portion of total mortality (approximately 8% according to a recent economic analysis of Canadian medical care costs). When non-accidental mortality or cardiovascular mortality data are selected, the percent increase in mortality (0.4% per 10 ppb) is statistically significant, and lower than the one observed for hospitalization data. This is reasonable, given that only a fraction of the population, likely those who have been severely ill, die during an ozone episode.

Farther down what has been referred to as the 'pyramid of effects' (American Thoracic Society 1985), two analyses of relationships of medical care required by asthmatics, one in Winnipeg and one in St. John N.B. (Stieb et al. 1995a,b), show that asthmatic individuals attended the Emergency Department about five times more frequently than they were admitted to hospital for respiratory disease. Doctors' visits were also shown to be more elevated than emergency Department visits, and days with reduced activity (absences from work or school) were also more frequent. The field studies also confirm that asthmatic attacks, symptoms, and medication use are increased in a significant portion of the population when photochemical smog is high. An independent analysis (Krahn et al. 1996) has recently confirmed this 'pyramid of effects', and gives some indication of the magnitude of effect that only a small percent increase in pollution, such as that calculated for ozone, would have on the health care system. Based on the analyses by Krahn et al. (1996), in 1990 in Canada, hospital-days for asthma (about 40% of all respiratory visits) were estimated to be 281,000, Emergency Department visits at 82,000 to 697,000 (depending on source of the estimate), physician services (based on two physician surveys) at 2 million to 3.6 million, and days in bed and off work or school at 2.1 million.

14.4.4 Susceptible population

Based on the exposure assessment using a pNEM model, a large portion of the general population is exposed to ozone concentrations above 82 ppb (current Canadian Ambient Air Quality Objective for 1-hour maximum ozone) for at least one day a year, and thus may be at risk from the adverse effects of ozone. Study of pNEM has also shown that in certain areas of Canada such as in Toronto, over 95% of the population has experienced at least one day a year of a 6- to 8-hour daily maximum ozone exposure above 50 ppb. This concentration has been shown to cause adverse effects in epidemiological studies. Moreover, some portions of the population are thought to be especially at risk from acute ozone exposure.

Patients with asthma and COPD have been shown to have significantly elevated levels of reactive oxygen species released from inflammatory cells (Rahman et al., 1996, Pratico et al., 1998), and a depletion of endogenous antioxidants (Rahman et al., 1996, Powell et al., 1994), causing imbalance of oxidants/antioxidants. Extensive production of reactive oxygen species and depletion of endogenous antioxidants in blood have also been documented in patients with cardiovascular diseases (Hoeschen, 1997, Mosca et a., 1997). Reactive oxygen species are known to be responsible for epithelial cell damage and mucus hypersecretion in respiratory tract, and myocardio and vascular endothelial lesions. It is conceivable that the imbalance of oxidants/antioxidants makes the patients more susceptible to the attack by exogenous oxidants such as ozone.

It is hypothesized that for individuals with asthma, allergy and COPD whose pulmonary function have already been compromised, further exposure to ozone may be enough to push them "over the edge", thereby exacerbating existing airway obstructions and limiting their ability to perform normal activities. This hypothesis provides a logical explanation for the observations in numerous population studies, employing several different endpoints, that serious health effects (increased medication use, emergency room visits, hospitalizations and mortality) have been demonstrated at levels well below those shown to cause effects in toxicological (animal) or clinical (controlled human exposure) studies.

It should be kept in mind that clinical studies have been conducted only on mild asthmatics and a few other sensitive groups, and no studies have been carried out on severely compromised cardio-pulmonary cases, for obvious ethical reasons. No studies have emphasized asthmatics or COPD patients with long duration of exposure. No airway inflammation data for COPD patients have been reported.

The second major group at risk comprises individuals whose activities outdoors lead to elevated ventilation rates. Cyclists, joggers, walkers, outdoor workers, and children would be included in this category. For example, lunchtime joggers would likely have a high ventilation rate, comparable to the heavily exercising individuals in some of the clinical studies, and be exposed at a time of day when ozone levels are at or near their daily peak in most parts of the country. This group is more at risk than sedentary individuals, because their high ventilation rates due to exertion may render a greater amount of ozone delivered to the target tissue in the lung per unit time, with a resulting greater drop in their FEV_1, greater possibility of inflammatory injury and greater development of symptoms (such as cough and chest tightness).

With respect to the age difference in response to ozone, clinical studies have shown that adolescents appear to be more sensitive to ozone-induced pulmonary function decrements when compared with adults using the same dose regimen. Older adults (60 years or older) have not been shown to be more susceptible to ozone-induced pulmonary function changes than their younger counterparts when given the same dose. Of the hospitalization studies that compared the effects of ozone on different age groups, most of them did not find that elderly people (>65 years) were more at risk than younger populations (<65 years). This suggests that age itself may not be a major determinant of response to ozone exposure, and that young adults may be equally sensitive to ozone as older adults.

14.4.5 Uncertainties

Exposure Issues

A majority of the epidemiological data considered in this document are ecological in nature, that is, results are based on populations, not on individuals, and the exposure of individuals to ozone is not known. In the time-series analysis, the assumption is made that the real exposures of the individuals in the population bear a constant relationship over time to the measurements from the ambient monitor(s). That is, the population average exposure, made up of the individual exposures of thousands or millions of people, will have the same relationship to the true exposure today as it had yesterday. Epidemiological studies often rely on a single fixed ambient monitor (FAM) to characterize the pollution levels in a given community. The concentration of ozone measured at that FAM is used as a surrogate for personal/population exposure without knowing what contact or degree of intake occurs. This may cause a mismatch of individual exposures and their health status. Therefore, in any ecological analysis, bias from exposure misclassification is a concern. However, the bias of differences in indoor versus outdoor concentrations within and between microenvironments, variability in daily time-activity patterns and life styles, and differences over time (several years) in mean exposures, is considered to be much less in time series studies than in cross-sectional (spatial) analyses. This is because time-series studies examine a single population longitudinally with respect to variations in exposure in an urban airshed over a short time. The population serves as its own control."

The ambient concentrations measured at the FAM are dependent upon the location of the monitor and its proximity to local sources. The locally generated ozone is superimposed on top of regional and long-range transport. Differences in local microclimate and the proximity to local sources or sinks may lead to pronounced concentration gradients. The reliability of exposure-response estimates is affected by the local spatial variability of ozone. If, for example, the monitors placed in the centre of the city indicate a high pollution level, while most of the population lives and spends most of the time in the suburbs where pollution levels are lower, then the wrong signal can be obtained from the results. The opposite can happen too. Central city monitors, where daily scavenging by NO_x takes place, may show very low ozone readings, while ozone may be high in the suburbs downwind of the sources. This pattern occurs in the Lower Fraser Valley, where ozone formation is in large part the result of local production, and concentrations are high up the Valley, while remaining low in the city centre. Therefore, to assure that ozone concentrations from FAMs better represent population exposures, the data from all FAM stations in the city can be averaged on an hour by hour basis.

Another problem regarding exposure is that the variation associated with an ozone risk estimate rises when exposure misclassification occurs. This can have the important impact of reducing or even eliminating the statistical significance of the exposure/outcome relationship. When analysing a mixture of pollutants, exposure misclassification can also bias the results toward the pollutant with the best and most accurate relationship of true exposure to measured exposure, by reducing the variance and thus increasing statistical significance of the result, as demonstrated by Lipfert & Wyzga (1995a).

Nonetheless, it is important to realize that the exposure status as determined from one or several ambient monitors is in many cases representative of the general population in the region. In the province of Ontario, much of the ozone is the result of broad regional air transport, and high correlations are observed between sites up to a hundred kilometres apart (Burnett et al. 1994). Personal exposure studies done in Canada (Brauer and Brook, 1995, Liu et al., 1995) and the US (Liu et al., 1993) also have shown that ozone data from personal exposure monitors were significantly correlated with the data from FAM. The central monitors are considered quite representative of the ambient exposure of the population served by each monitor.

Confounding Factors

In some locations where temperature was highly correlated with ozone ($R \geq 0.5$-0.6), it was a potential confounder, since it could itself be associated with increased respiratory distress (at both high and low temperatures). The method of handling temperature in the statistical analysis is therefore important, with inclusion in the regression appearing to provide the most reliable results. Fortunately, a majority of time-series studies have used this or other methods to adjust the effect of temperature on both health outcomes and ozone concentrations. On the other hand, removal of the temperature effect prior to running the regression with ozone carries with it the risk of removing part of the ozone effect in cases where correlation between them was moderate or high, as is often the case in summer, and thus may lead to an underestimate of ozone effects.

Airborne pollution always occurs as a mixture of agents, of which ozone is only one. Particulate matter has been the co-occurring pollutant of greatest concern with respect to confounding of the relationship between ozone and adverse health endpoints. Particulate matter (PM) is independently associated with adverse health outcomes including mortality, hospitalizations and Emergency Department visits, from cardiovascular as well as respiratory causes. Therefore, if unadjusted, part of the health effects found associated with ozone may in fact be attributed to PM. The degree of correlation between various metrics of PM and ozone is somewhat dependent on the location, i.e., on the relative role of local sources versus long-distance transport via movement of entire air masses, seasonal effects, etc. Additional difficulties with the inclusion of PM in analyses are presented by the variety of metrics that have been used to measure it, and some controversy over which size of particle is responsible for the observations of adverse health effects. Further major difficulties are presented by the 6-day monitoring schedule for PM followed almost universally throughout North America, which has made it difficult or impossible to include PM in regression analyses for daily changes in pollutants compared to daily changes in adverse health outcomes. Similarly, other co-occurring pollutants often, but not always, have long-term fluctuations in levels. Many authors have not investigated the modifying effects of one or more of NO_2, SO_2, or CO on outcomes associated with ozone, although measurements were often available. In this document, in order to overcome the confounding effects of co-pollutants in time-series studies, a list of criteria was established to ensure that the data used for generating average relative risks for ozone are from studies applying multi-pollutant models. The health effect data were weighted by their variances, which provide an indication of how well the means represent the population values.

Subjects and Endpoints Used

Previous standard setting processes have been mostly influenced by the effect of ozone on pulmonary function. However, there exists evidence from clinical studies that O_3-induced changes in FEV_1 do not correlate with cell injury endpoints and bronchial hyperresponsiveness. It is still not certain whether spirometric parameters are the right indicators for ozone toxicity (i.e. at which point a decrement in FEV_1 reflects injury).

It should also be noted that clinical studies have been conducted only on healthy people and people with mild respiratory problems, and no studies have been carried out on severely compromised cardio-pulmonary patients, for obvious ethical reasons. No studies have examined asthmatics or COPD patients under conditions of long exposure duration. No airway inflammation data for COPD patients have been reported. All the clinical studies have been conducted using ozone concentrations above 80 ppb.

Research Needs

The discussion above indicates that more scientific research is required, in a number of critical areas, in order to fill the knowledge gaps:

- Effort should be made to develop methodologies that make full use of pNEM data, which integrate detailed information on human activity patterns, indoor-outdoor ratios of ozone concentrations, and air exchange rates, to predict personal exposure for use in epidemiological studies. Field (camp or panel) studies may be conducted using personal exposure monitors to investigate the relationship with health outcomes.

- Since most Emergency Department visit studies have had limited databases, and investigated only asthma-related visits, future ED visit studies need to expand their databases, and include ED visits for other cardio-respiratory diseases.

- There are only limited data on chronic health effects of ozone, and most of them are from cross-sectional studies. More longitudinal studies should be conducted to examine the long-term effects of ozone exposure.

- More sensitive biological markers need to be developed to examine tissue injury rather than functional changes, in field studies and controlled exposure (clinical) studies. Field or clinical studies with more sensitive biological markers may also help to shed some lights on the mechanism of the association between ozone and cardiac mortality.

- Clinical data on ambient-levels of ozone-induced pulmonary injury are very limited, and need to be expanded to corroborate the findings in epidemiological studies. More systemic studies, such as those investigating cardiovascular effects, should also be carried out to elucidate the mechanisms of ozone-induced cardiovascular mortality observed in epidemiological studies.

- It is not clear how animals with pre-existing cardio-respiratory disease respond to ozone exposure. It is desirable to examine the effects of ambient levels of ozone on animals with compromised cardio-respiratory systems. More systemic effects, such as cardiovascular and developmental effects, should be investigated to elucidate the mechanism(s) of ozone-associated cardiovascular mortality observed in epidemiological studies.

- Much clinical work needs to be carried out to assess the effects of air pollutant mixtures. So far, few studies have included more than two chemicals, and the endpoints measured are often limited to pulmonary function variables.

14.4.6 Weight of evidence for ozone as a cause of adverse respiratory health effects (weightings to be assigned to the three types of study)

There are several reasons for weighting the epidemiological studies more than the controlled human exposure studies or animal toxicological studies when evaluating levels of exposure that result in adverse health effects. (1) Epidemiological studies addressing the acute and chronic health effects in human populations involve those combinations of environmental conditions and activity levels present under real-world conditions of ozone exposure. This real-world relevance is an advantage over animal and controlled human exposure studies. (2) Urban populations are highly heterogeneous, including individuals who encompass a large range of susceptibilities, disease status, and exposures. Their responses cannot be predicted from classical animal toxicology or even controlled human exposure (clinical) studies. Population (ecological) studies using very large administrative databases are likely to capture a greater range of responsiveness, including those responses from the tail end of the distribution curve. (3) Population-based epidemiological studies are predominantly time-series studies, which are longitudinal and use a single population as its own control, and thus are less vulnerable to inter-population bias. (4) Since the purpose of such time-series epidemiological analyses is usually to help set ambient standards that will ultimately be monitored at central stations (FAM), the use of FAM data in the original epidemiological studies simplifies the standard-setting process (i.e., thereby avoiding any extrapolation between individual exposures measured during research and FAM monitor concentrations to be employed in standards-compliance monitoring). On the other hand, because of the use of FAM data, a significant drawback associated with ecological studies is the lack of knowledge about which individuals in the population respond when the ambient monitor measures the ozone level, i.e., what were the ozone exposures of the individuals who were hospitalized, visited the emergency department, or died. Nevertheless, personal monitoring studies conducted in Canada and in the US have demonstrated that mean personal exposures to ozone have the same temporal trend as the FAM concentrations, suggesting that ozone data from FAM can represent population exposure.

Controlled human exposure (clinical) studies can provide valuable information about the threshold of a specific effect, at ambient exposure concentrations, to a single pollutant or to the joint effects of two pollutants, but not to the complex mixtures experienced in most ambient locations. Clinical studies also are valuable in providing quantitative information on the response to ozone in normal individuals and in individuals who have pre-existing respiratory disease (e.g., asthma) or atopy. Information on susceptible groups cannot be obtained from an ecological study based on population responses as captured in large administrative databases. Information on airway responsiveness, lung function changes, inflammatory responses, and symptomology after known doses of ozone can and have been obtained from clinical studies, and provided insight into the mechanisms underlying the observations in the epidemiological studies on population health. However, most of the data reported in the clinical studies have been gathered from studies that were performed under very similar conditions, with a small sample size, and with only a few studies using individuals with pre-existing respiratory diseases (mild asthmatics), or very young/old subjects. No study on tissue injury has been reported under 80 ppb of ozone for healthy subjects, or under 120 ppb of ozone for asthmatics. These drawbacks limit the use of clinical data for predicting the health effects in a general population and for obtaining a LOAEL or NOAEL.

Animal studies are valuable in elucidating cellular changes and mechanisms of action of ozone. They are particularly valuable in relation to the possible effects of long-term exposures, because controlled human exposure studies over a long period of time are impractical, and epidemiological studies on chronic endpoints are as yet too few to draw conclusions regarding chronic effects. The animal experiments also add support to the biological plausibility of the observations from clinical and epidemiological studies. Comparative dosimetric studies have provided evidence that humans receive four to five times more ozone in their lower airways than rats do, when given the same dose. Following deposition in the deep airways, animals and humans have been shown to have a similar tissue dose - effect relationship (lung injury), on a per unit body weight basis. Given that ozone as low as 100 ppb has been demonstrated to cause rat pulmonary inflammation, this is equivalent, in terms of inducing an effect, to human exposures of 20-25 ppb, based on the observations made above. On this basis, the doses used in rats are clearly relevant to the concentrations encountered by human populations at current ambient levels of ozone. So far, there has only been a limited number of comparative dosimetric studies carried out, which precludes establishing a human LOAEL or NOAEL for ozone by using animal toxicological data.

With respect to characterizing a susceptible subpopulation, as discussed above, epidemiological (ecological) studies do not tell us exactly who is responding to ozone, although some studies on Emergency Department visits focused on asthma as an target group. The respiratory-related hospital admissions were noted for at least three categories of respiratory illness, of which asthma constituted 35-40%, and the remaining 60-65% were from infections and non-asthma-related illnesses including respiratory bronchiolitis. The clinical studies support the findings that asthmatics may be more susceptible, since their lung function has shown decrements under certain conditions before these are seen in normal individuals. An important clinical finding with respect to causality relates to the nature of asthma, which has now been shown to be an inflammatory disease involving epithelial destruction in the respiratory tract. Asthmatics, and a certain proportion of the normal population without overt symptoms of asthma, have been found to be hyper-responsive when challenged with a bronchial constrictor such as methylcholine. These hyper-responders react to airborne pollutants, including ozone, to a greater extent than normal-responders. The clinical studies thus provide a foundation to support the thesis that certain groups of people, such as asthmatics, are more sensitive to ozone toxicity.

Animal studies were the first to demonstrate the link between ozone exposure and immunotoxicity mediated through damaging alveolar macrophage function, thus impairing defence mechanisms in the lung. Animal studies have demonstrated ozone-inflicted deaths in mice with bacterial infection such as *streptococcus zooepidemicus* or influenza bacteria. The epidemiological findings that infection-related illnesses are linked to peak ozone exposure are thus supported as being biologically plausible.

Taken together, the animal toxicity studies, the clinical studies, and the epidemiological studies provide a coherent picture of ozone-induced inflammation of the respiratory tract, destruction of cells involved in the immune defence system of the lungs, and triggering of hyper-responsive bronchi in asthmatics and others. The responses initiate a cascade of effects progressing from reduced activity, absences from work/school, and physician visits, to Emergency Department visits, hospitalizations, and even death.

The existence of this cascade is supported by the estimated risks for a given ozone concentration, which increase from mortality (0.4% per 10 ppb), to respiratory hospitalizations (1-2% per 10 ppb), to respiratory ED visits (6-8.5% per 10 ppb). The pyramid pattern of health effects is also supported by an independent assessment of the costs to the Canadian health care system of asthma (Krahn et al. 1996), which have increased as a result of either an increase in the prevalence or severity of asthma during the 1980s, based on increased demands for medical services (Wilkins & Mao 1993). Krahn et al. (1996) examined inpatient care (hospitalizations), emergency visits, an audit of practice patterns of office-based physicians, drug prescriptions, and two population based surveys on health to estimate costs for one year, 1990. They found: 550 deaths, 281,000 hospital-days (the average stay <3 days), 182,000- 697,000 Emergency Department visits, 2,000,000 -3,600,000 physician services, 1,300,000 days lost due to disability, 800,000 school days lost, and 3 to 6 million reduced activity days, all attributable to asthma. Since asthma is a multifactorial disease, or perhaps a group of diseases, air pollution could have been responsible for only a small portion of these effects, but the attributable risk becomes very large when the entire country is considered over a period of a year. In addition, it should be remembered that asthmatics are only one of several groups in the population at risk of respiratory damage due to ozone.

14.4.7 Conclusions

Ground-level ozone is formed when its precursors, nitrogen oxides and volatile organic compounds, combine in the presence of sunlight. Ozone is one of several pollutants that combine to form a chemical soup that hangs in the warm, still air over many Canadian cities on hot summer days. Scientific evidence clearly links ozone and health impacts. As a mixture, and individually, these air pollutants have the potential to cause adverse health effects.

The population-based epidemiological studies have provided a consistent and coherent evidence of an exposure-response relationship. Non-accidental mortality, hospital admissions, Emergency Department (ED) visits and reduced activity days increase monotonically as ozone concentration increases. Increased risks for non-accidental mortality, respiratory hospitalization and ED visits respectively are estimated at 0.4%, 1-2% and 6-8.6%, for every 10 ppb increase in ozone. The risks of population health effects increase monotonically, in a ozone concentration-dependent fashion. The controlled human exposure studies have identified a dose-response relationship for lung function changes, symptoms and airway inflammation, the frequency and intensity of response increasing with increases of ozone concentration, exposure duration or ventilation rate. Field (camp and panel) studies and controlled human exposure studies have identified that patients with asthma, COPD and allergic rhinitis are more susceptible to ozone-induced health effects than healthy people. Animal toxicological studies, used qualitatively, have provided evidence of mechanisms for acute and chronic effects of ozone, including mortality. Dosimetric studies of humans and animals have helped to establish a linkage for the use of animal data in predicting ozone effects on humans, and have suggested that ozone doses used to induce various tissue injuries and deaths in animals are relevant to the concentrations encountered by human populations.

Combining the information, there is convincing evidence of a significant association between ambient ozone and adverse health effects. Evidence suggests a biologically plausible mechanistic sequence(s), beginning with an inflammatory response which irritates the respiratory tract, giving rise to cough, pain which inhibits inspiration, and bronchoconstriction which reduces airflow. The inflammatory response also damages the cells lining the respiratory track, which increases lung permeability and could lead to lung edema. Ozone-induced impaired endogenous defence system (including injury of immune cells and depletion of antioxidants) would render the individual more vulnerable to viral or bacterial infections. These effects and symptoms, if severe enough, could lead to respiratory dysfunction and a requirement for medical intervention such as doctor or emergency room visits, and hospitalization. Although more data are required to fully explain the mortality associations, it is logical to expect that the biological stress related to these effects could exacerbate underlying conditions (e.g. cardiovascular problems) and lead to acute death. The inflammatory portion of the cascade of effects can be present with or without the accompaniment of pulmonary function changes depending on the sensitivity of the individual.

Results from controlled exposure studies of respiratory patients, along with the epidemiological evidence of hospitalizations, emergency room visits, and reduced activity days, suggest that people who are compromised by pre-existing respiratory diseases are more susceptible to ozone exposure.

Controlled human exposure studies indicate exercise is a potent modifying factor in the response. For a given concentration and duration of ozone exposure, the effect is strongly dependent on the level of exercise, because exercise enhances the ventilation rate and consequently the dose delivered to the lower airways. Results from field studies using lunchtime joggers or competitive bicyclists support this finding.

Estimates of population exposure indicate that large numbers of people are exposed to low levels of ozone in Canada (below the current National Ambient Air Quality Objective). Although ambient ozone levels are higher than personal exposure data, they share the same temporal pattern, suggesting that ambient ozone data used in epidemiological studies can be an effective indicator for population exposure. It is also clear that at concentrations currently experienced in Canada, population health effects (mortality and morbidity) are occurring. The increase in unmeasured morbidity (cough, substernal soreness, increased airway reactivity, increased asthmatic attacks, increased medication use) is substantially greater than the measured outcomes from administrative databases (such as hospitalizations, Emergency Department visits).

Newly published data suggest that there likely exist health effects (pulmonary function decrements and induction of new asthma cases) from chronic exposure to ozone. Future development of air quality policy for ozone may require inclusion of an annual or seasonal objective, since this may be more important in much of Canada where chronic low exposure are more prevalent than short peaks.

The acute effects are by definition related to peaks in ozone levels, with the clinical and population health studies correlating responses with hourly or multi-hour (6 - 8 hour) exposures. Available data did not show a substantial difference in the association of health effects with 1-h maximum ozone or 8-hour average ozone levels. This is expected given the high correlation between 1-hr daily maximum and the maximum 6- or 8-hr concentrations. It is noteworthy that a clinical study using varying doses as well as a constant dose over 8 hours (with the same total concentration) has demonstrated that the subjects responded in terms of pulmonary function decrements almost twice as markedly to the varying dose regimen as to the constant dose of ozone. These results suggest that the average dose value calculated as a mean over an 8-hour exposure may underestimate the effect of ozone on pulmonary function induced by a peak exposure.

An averaging time of 24 hours is not considered a best choice of metric because of the strong diurnal pattern exhibited by ozone and the substantial year to year variation in ozone maxima at different sites across the country. Therefore, the averaging time of any target level needs to be less than 12 hours. In view of the results from most Canadian studies, and from controlled human exposure studies showing effects on lung function after an exposure (0.16 ppm) as short as 1 hour (with continuous vigorous exercise), a slight preference is expressed for retention of an 1-hour averaging concentration.

14.4.8 Recommendations

The data show that there is a significant association between ambient ozone concentrations and health effects. These associations have been demonstrated in epidemiological studies, and a causal relationship has been supported through human clinical studies and animal studies. The risks associated with increases in ambient ozone concentrations and health effects such as mortality and hospitalization have been examined in a number of studies covering cities across the world. The regression analyses performed on 13 Canadian cities represent the ozone effects across Canada. The results are similar to those observed in studies of cities across the world. Because the 13-Canadian city study (Appendix A) is, for the time being, the only study that has appropriately established LOAELs for the health effects of the Canadian population in comparison with other approaches, it was recommended that the results from these analyses be used as the basis for determining Reference Levels for ozone (Chapter 13). For risk and benefit analyses, however, it is recommended that the estimates of risk derived from meta-analyses, using studies worldwide, be used, since these studies have adjusted for possible co-pollutant effects. It must be kept in mind that adjusting for co-pollutants using multi-variate models tends to underestimate the risk attributable to ozone, as ozone and other co-pollutants are often statistically correlated.

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APPENDIX A

Estimating a "National Reference Level" for Ozone in Canada

(Burnett, 1998)

Estimating a "National Reference Level" for Ozone in Canada

March 5, 1998

Purpose:

The well established statistical association between hospital admissions for respiratory illnesses and daily one hour maximum ozone levels was used as the bases to determine the *National Reference Level* (NRL) which is defined as "the lowest ambient concentration of ground level ozone that can be statistically associated with an adverse health outcome". The association between ozone and non-accidental mortality is also examined.

Methods:

The strongest statistical association with an adverse health outcome observed at low concentrations in Canada is for hospitalization for respiratory illness such as asthma, objective lung diseases, and pneumonia. To that end, the daily number of admissions to hospital for acute bronchitis (ICD9 466), pneumonia (480-486), and chronic obstructive pulmonary disease (490-496) were obtained from Statistics Canada's national hospitalization database for the period April 1, 1981 to December 31, 1991 for the following cities: Vancouver, Edmonton, Calgary, Winnipeg, Windsor, London, Hamilton, Toronto, Ottawa, Montreal, Quebec City, Saint John, and Halifax. Concurrent daily concentrations of the one hour maximum level of ground level ozone were also obtained from the NAPS database, in addition to daily readings of maximum and minimum temperature, daily average dew point temperature, and daily average relative humidity.

There now exists a mounting body of epidemiological evidence that suggests that ozone may also be related to non-accidental mortality. In order to examine this association, the daily number of deaths due to non-accidental causes (ICD9 < 800) for the period January 1, 1980 to December 31, 1991 were also obtained for the 13 Canadian cities and compared to concurrent levels of ozone.

In order to compare daily variations in ozone levels and daily fluctuations in admission or mortality rates both the event and ozone time series were adjusted for long term trends and seasonal variations using non-parametric smoothed functions of day of study, and day of the week differences for each city separately. These smooth functions remove any low frequency cyclic patterns and non-cyclic trends in both the event and ozone data that might obscure the true association between daily variations in both time series. On any given day, the pre-filtered event or ozone data represent deviations from a average value based on data near that day. In this analysis, a 31-day span of the smoother was used. Thus the pre-filtered data represent differences between the observed data and a (weighted) average of data on the specified day and 15 days in the past and 15 days in the future. The pre-filtered data will not necessarily have the same stochastic structure as the original values. For example, suppose on a certain day the ozone level is 100 ppb and the average ozone concentrations in the 31 day period around this day is 80 ppb. Further consider a day in which the average ozone value is 40 ppb and is surrounded by an average ozone level of 20 ppb. The pre-filtered values on both days are 20 ppb yet the absolute value of ozone is quite different. Pre-filtering not only removes potentially confounding temporal patterns but also normalizes the data among cities. The city-specific pre-filtered data measures deviations from each city's specific temporal pattern. A change of 10 ppb in Vancouver can be combined with a 10 ppb change in ozone in Halifax controlling for the confounding influences of potentially quite dfferent temporal patterns of ozone levels in each city.

City-specific weather effects were also removed from the admission time series. This was accomplished by modeling the effects of daily maximum and minimum temperature, daily average dew point temperature and daily average relative humidity recorded on the day of, and one and two days prior to the day of admission using non-parametric smoothed functions. Temporal trends and day of the week effects were removed from the ozone series in order to reduce the confounding effects of these cycles.

The city-specific pre-filtered events (admissions or deaths) were merged among all 13 cities and compared with the merged pre-filtered ozone data. Pre-filtered ozone levels recorded on the event day and 1 to 4 days prior to the event day were related to the pre-filtered event time series. The lagging period with the strongest association with the event series was used to determine the NRL.

The lowest concentration for which a statistically significant association can be observed between pre-filtered ozone and the pre-filtered event series was determined by regressing pre-filtered ozone on the pre-filtered events using datasets in which all days with original ozone concentrations above selected values were removed from the analysis. Restrictions were based on days with the original ozone levels and not on the pre-filtered values. Relative risks and standard errors were obtained using Generalized Additive Models in which the residual variance is proportional to the expectation, thus accommodating over(under) dispersion relative to Poisson variation.

The NRL is defined as the lowest concentration for which a regression analysis of data which did not include days on which the ozone concentration was above this value yielded a positive and statistically significant association with the event series among the lagging periods examined. This should not be interpreted as a threshold level, but the lowest concentration above a threshold, if it exists, for which we are confident that a statistical association between ozone and either hospitalizations for respiratory diseases or non-accidental deaths exists in Canada.

Both pre-filtered event and ozone data were combined among cities in order to determine a NRL. City-specific "Reference Levels" were not determined since this approach would yield a reduction in statistical power to detect the minimum concentration in which a statistically significant association could be detected in each city separately due to the smaller city-specific event rates compared to the event rate in the combined sample. Further, there is a distribution of such concentrations among cities, and it is not clear what characteristic(s) of this distribution would be appropriate to select a NRL. One could select some measure of central tendency, such as the mean or median. However, this concentration would not be indicative of all regions in Canada. The minimum city-specific concentration could also be selected, but this value may be region specific and would not incorporate data from other parts of Canada. The method of combining data among cities to determine the NRL has the advantage of increased statistical power over the city-specific approach and also utilizes information from all regions of the country.

Results:

City-specific daily admission rates for respiratory diseases and non-accidental mortality rates, study average one hour maximum ozone concentrations and their 99th percentile values are given in Table 1, in addition to the optimal weather model. The optimal weather model was selected using a forward inclusion stepwise regression procedure with the 12 weather predictors (daily maximum and minimum temperature, daily average dew point temperature, and daily average relative humidity, each recorded on the day of and one and two days prior to the date of admission). The minimum set of these 12 weather predictors which explained the largest amount of residual variation in event rates with the least number of predictive variables was selected as the optimal weather specification for each city. The stepwise procedure was used since the weather variables can be highly correlated and inclusions of several correlated variables in a regression analysis artificially inflates the standard error of the other variables in the model, i.e. ozone.

The percentage increase in hospital admissions for respiratory diseases or non-accidental mortality attributable to a 10 ppb increase in the daily maximum one hour ozone concentration among 13 Canadian cities is given in Table 2 for the ozone levels recorded 0, 1, 2, 3, and 4 days prior to the event date.

Risk of hospitalization increases from 0 to 2 days lagged and then decreases to 4 days lagged. [The median time between onset of respiratory symptoms and presentation at the emergency department in Saint John NB is two days.] The strongest association between ozone and non-accidental mortality was for concentrations recorded on the day of death. [The median time between onset of heart problems and emergency department visits was 0 days. Heart problems are common immediate causes of death.]

The regression analysis was repeated after removing days in which the daily one hour maximum ozone concentration was above selected values. The increased percentage of respiratory hospital admissions or non-accidental mortality corresponding to a change in ozone of 10 ppb are given in Table 3 for selected concentration restrictions. Ozone risks for respiratory hospitalizations tend to decrease slightly from 1.04%, using all the data, to 0.74% if ozone values above 25 ppb are not included in the analysis. If days on which ozone concentrations are above 20 ppb are excluded however, the risk is clearly reduced. The risks are less sensitive to removal of high ozone concentrations for the mortality data.

Strong statistical evidence for an positive association is defined for the purposes of this analysis when the ratio of the risk to its standard error (T-ratio) is greater than 2.33, based on a one sided type I error rate (p-value). This corresponds to a p-value of 0.01. [The one sided test is used since ozone is expected to be positively associated with respiratory hospital admissions and non-accidental mortality and thus only positive associations are relevant.] The lowest concentration corresponding to T-values greater then 2.33 is defined as the Lowest Observed Adverse Effect Level (LOAEL).

Discussion:

The LOAEL is 25 ppb if based on respiratory hospital admissions and is 20 ppb based on non-accidental mortality.

The ozone risk for hospital admissions for respiratory diseases is 1.04% /10 ppb increase in daily one hour maximum ozone with a 95% confidence interval of 0.78% - 1.30%. The risk for non-accidental mortality is 0.79% (95% CI: 0.59% - 0.99%).

There is some evidence of a threshold concentration with respiratory hospitalizations. A positive risk was observed for ozone concentrations below 20 ppb (0.31%) and a negative risk for ozone values below 15 ppb (-0.29%). No such evidence for a threshold was observed with the mortality data.

Excess deaths attributable to ozone exposure were determined after controlling for temporal trends in both the event rates and ozone concentrations, day of the week effects, and weather predictors. However, the potentially confounding effects of other ambient air pollutants were not accounted for in this analysis.

It has previously been shown that carbon monoxide, nitrogen dioxide, and sulphur dioxide did not confound the association between ozone and respiratory hospitalizations in 16 Canadian cities (Burnett *et al*, 1994: *Environmental Research*, 72, 24-31), nor was the association between ozone and mortality confounded by adjustment for these gaseous pollutants in 11 Canadian cities (Burnett *et al.*, 1998: *Canadian Journal of Public Health*, May/June issue - to appear).

Daily measures of particulate mass which are known to be related to both respiratory hospitalizations and mortality were not available for the 13 cities examined here. Ozone tends to be negatively correlated with fine particulate mass in the winter months, uncorrelated in the spring and fall, and positively correlated in the summertime in Canadian cities. Ozone and fine particles are uncorrelated if the entire year is examined. Fine mass could be a confounder to the effects of ozone in the summer months. Ozone remained a positive risk factor for summertime respiratory hospitalizations in 168 acute care hospitals in southern Ontario after controlling for particulate sulphates (Burnett *et al*, 1994: *Environmental Research*, 65, 172-194), and for summertime respiratory hospital admissions in Toronto after controlling for fine and coarse particulate mass (Burnett *et al*, 1994: *Environmental Health Perspectives*, 105, 614-620). There is thus some evidence of an effect of ozone on respiratory hospital admissions independent of gaseous and particulate pollution. However, there have been no Canadian studies that have adjusted the ozone effect on mortality for particulate mass. We can only conclude that the ozone effect on mortality is likely to be independent of the effects of the other gaseous pollutants.

Table 1. City specific population, variables in weather model, daily mean event rate and study mean and 99th percentile value of ozone concentration.

City	Pop* (x 10^{5})	Weather Model$^{\bullet}$		Event Rate/Day		Ozone Concentration	
		Deaths	Admissions	Deaths	Admissions	Mean (ppb^{++})	99th Per. (ppb)
Halifax	3.1	MaxT$_0$	RH$_0$, DP$_1$	4.9	5.6	27	64
Saint John	1.4	RH$_0$, RH$_2$	RH$_2$	2.7	3.1	37	87
Quebec	5.7	MinT$_1$	RH$_2$	9.4	9.3	27	70
Montreal	24.6	DP$_0$, RH$_2$	DP$_1$	46.1	29.1	28	78
Ottawa	8.0	RH$_2$	MaxT$_0$	11.6	11.5	26	69
Toronto	31.4	DP$_0$, RH$_2$	DP$_0$	50.3	45.0	30	87
Hamilton	4.2	MaxT$_0$, MinT$_2$	RH$_0$	8.5	5.7	34	90
London	3.3	DP$_0$, MaxT$_1$	RH$_0$	6.6	4.8	38	96
Windsor	3.2	MinT$_0$, MaxT$_2$	MinT$_0$, RH$_0$, RH$_2$	6.7	6.1	38	103
Winnipeg	5.9	RH$_2$	MinT$_0$	12.0	9.8	31	65
Edmonton	7.2	RH$_1$	MinT$_0$, MaxT$_2$	9.8	13.0	30	65
Calgary	8.1	MinT$_0$	MinT$_0$	8.6	5.7	33	65
Vancouver	14.0	MinT$_2$	DP$_0$, RH$_2$	26.6	20.6	25	64
Average	9.85			15.6	13.0	31	

*Based on 1986 census.

• : RH - daily average relative humidity, DP - daily average dew point temperature, MaxT - daily maximum

temperature, MinT - daily minimum temperature. Subscript refers to number of days between recording of variable and event date.

++ ppb - parts per billion.

Table 2. Percentage increase in hospital admissions for respiratory illnesses or non-accidental deaths attributable to a 10 ppb increase in daily maximum one hour ozone concentration among 13 Canadian cities by days lagged (T-ratio given in parenthesis).

	Event	
Days Lagged	**Admissions**	**Deaths**
0	-0.02 (-0.16)	0.79 (7.57)
1	0.79 (5.93)	0.65 (6.18)
2	1.04 (7.79)	0.38 (3.66)
3	0.64 (4.83)	0.16 (1.61)
4	0.18 (1.36)	-0.15 (-1.46)

Table 3. Percentage increase in respiratory hospital admissions or non-accidental deaths attributable to a 10 ppb increase in the daily maximum one hour ozone concentration by amount of ozone data remaining the regression analysis (T-ratio given in parenthesis).

Observations Excluded	Percentage of Observations Remaining	Event	
		Admissions	Deaths
None	100	1.04 (7.79)	0.79 (7.57)
>50 ppb	89	0.97 (6.45)	0.85 (6.03)
>45 ppb	85	0.88 (5.65)	0.81 (5.50)
> 40 ppb	78	0.91 (5.50)	0.81 (5.15)
> 35 ppb	68	0.87 (4.78)	0.77 (4.57)
> 30 ppb	56	0.78 (3.83)	0.78 (4.25)
>25 ppb	40	0.74 (3.04)	0.79 (3.58)
> 20 ppb	26	0.31 (0.99)	0.92 (3.14)
>15 ppb	13	-0.29 (-0.65)	0.63 (1.37)
> 10 ppb	5	-0.17 (-0.24)	0.53 (0.07)